

BEST AVAILABLE COPY

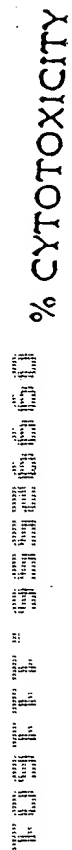


FIG. 1

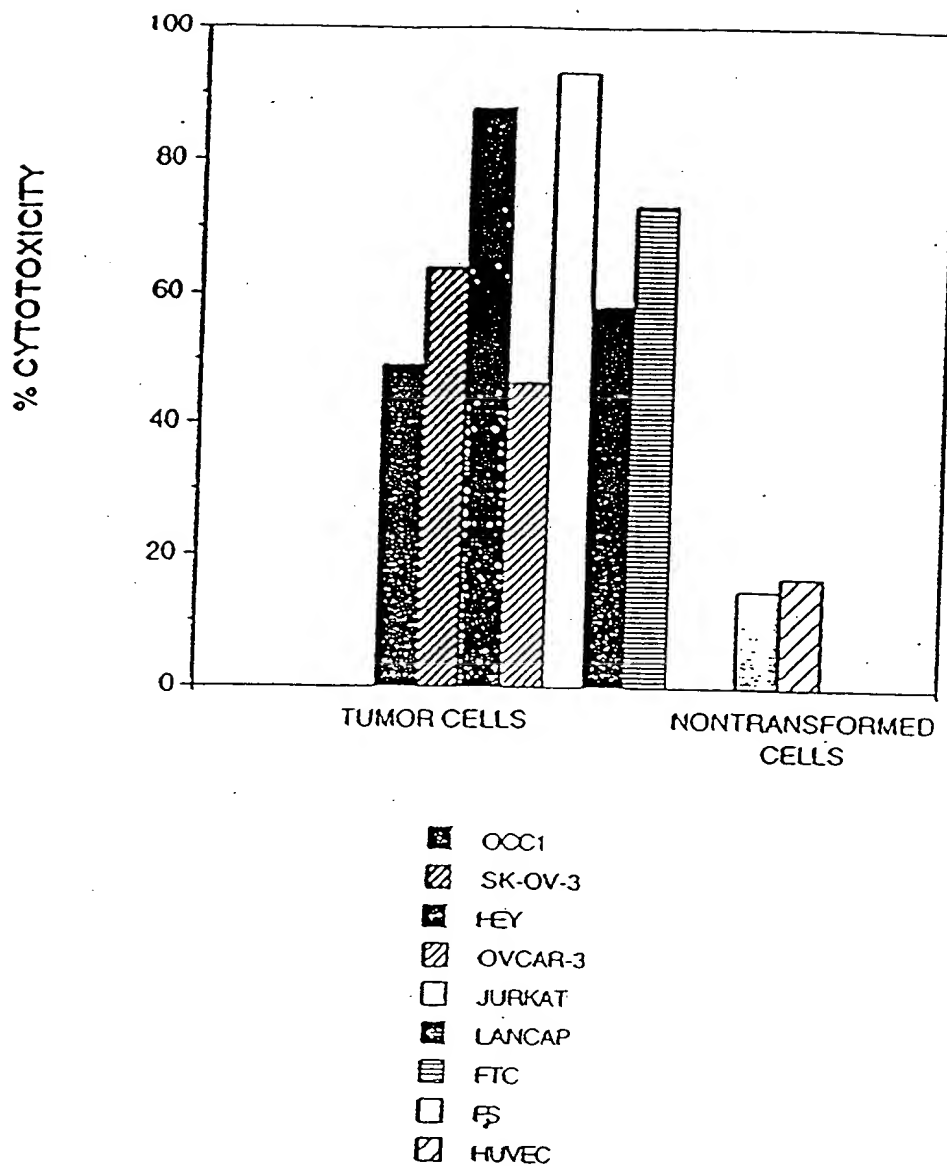


FIG. 2

TOP SECRET 9552660

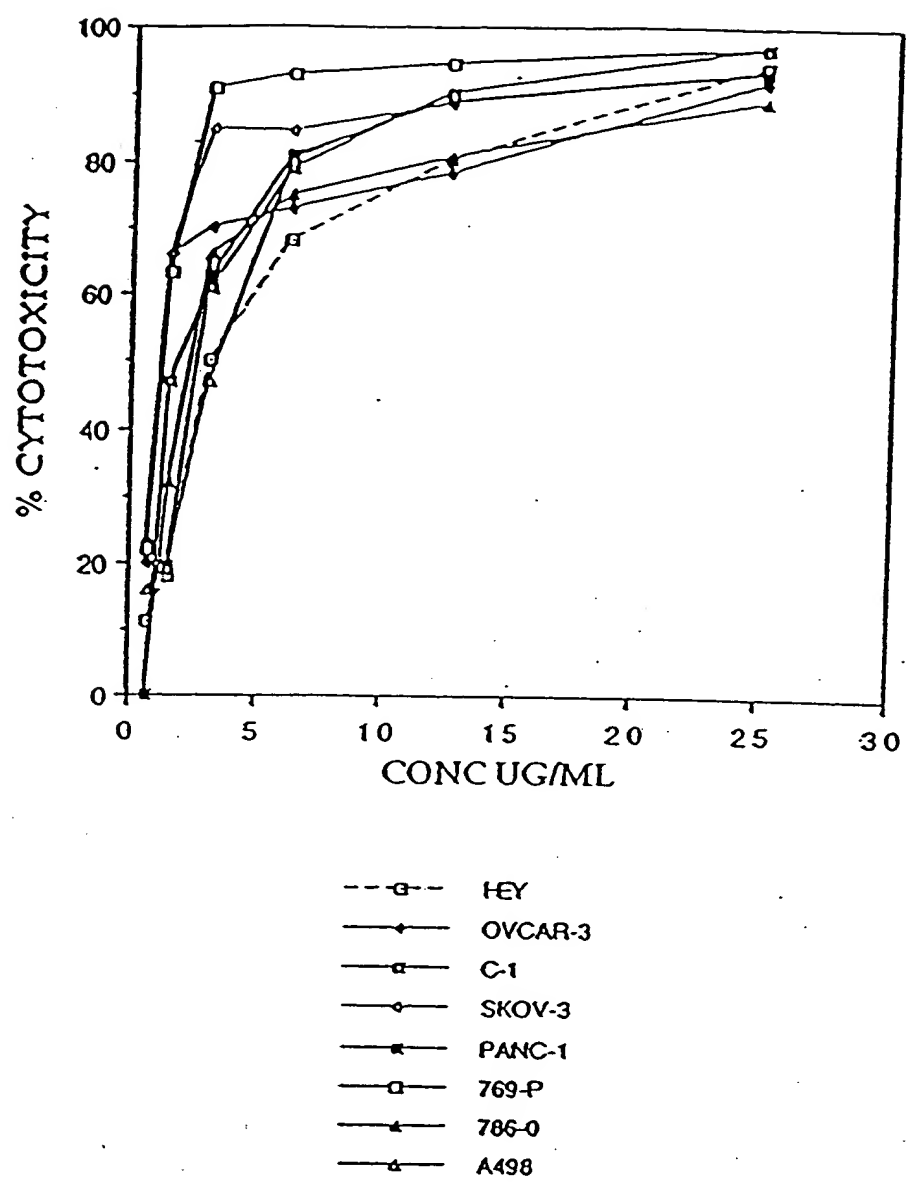


FIG. 3

TOP SECRET

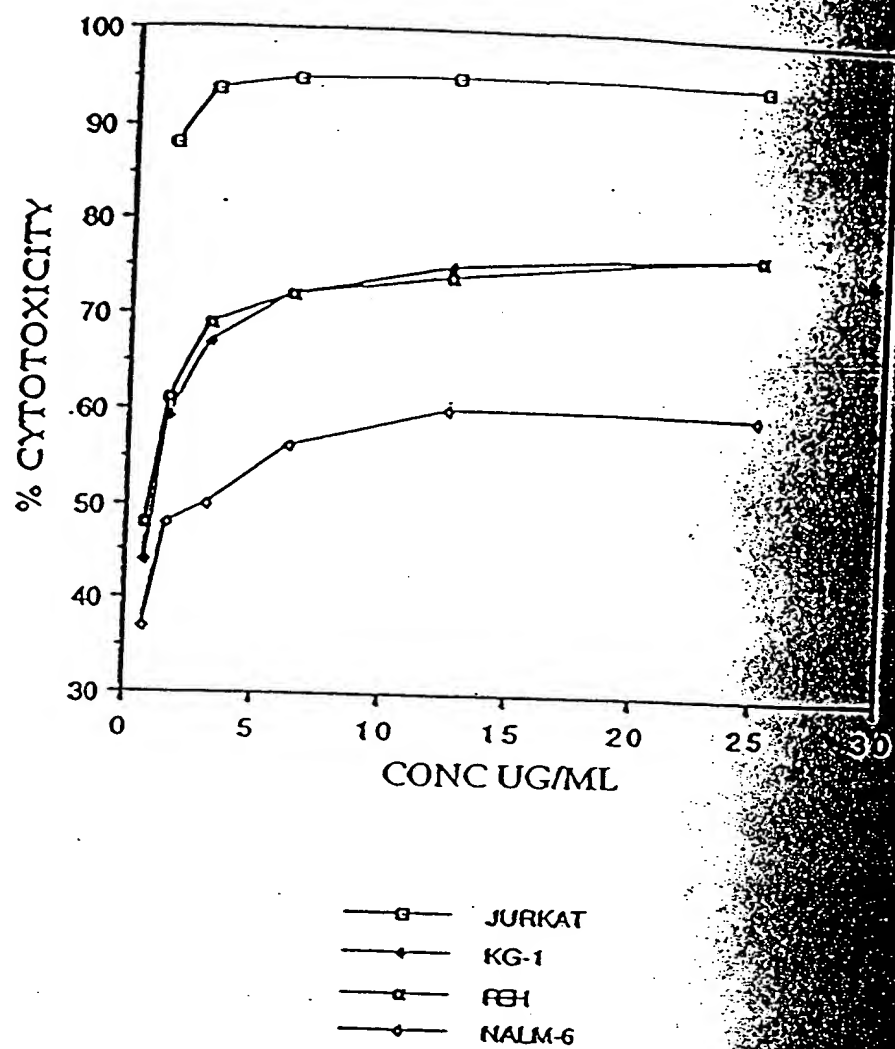
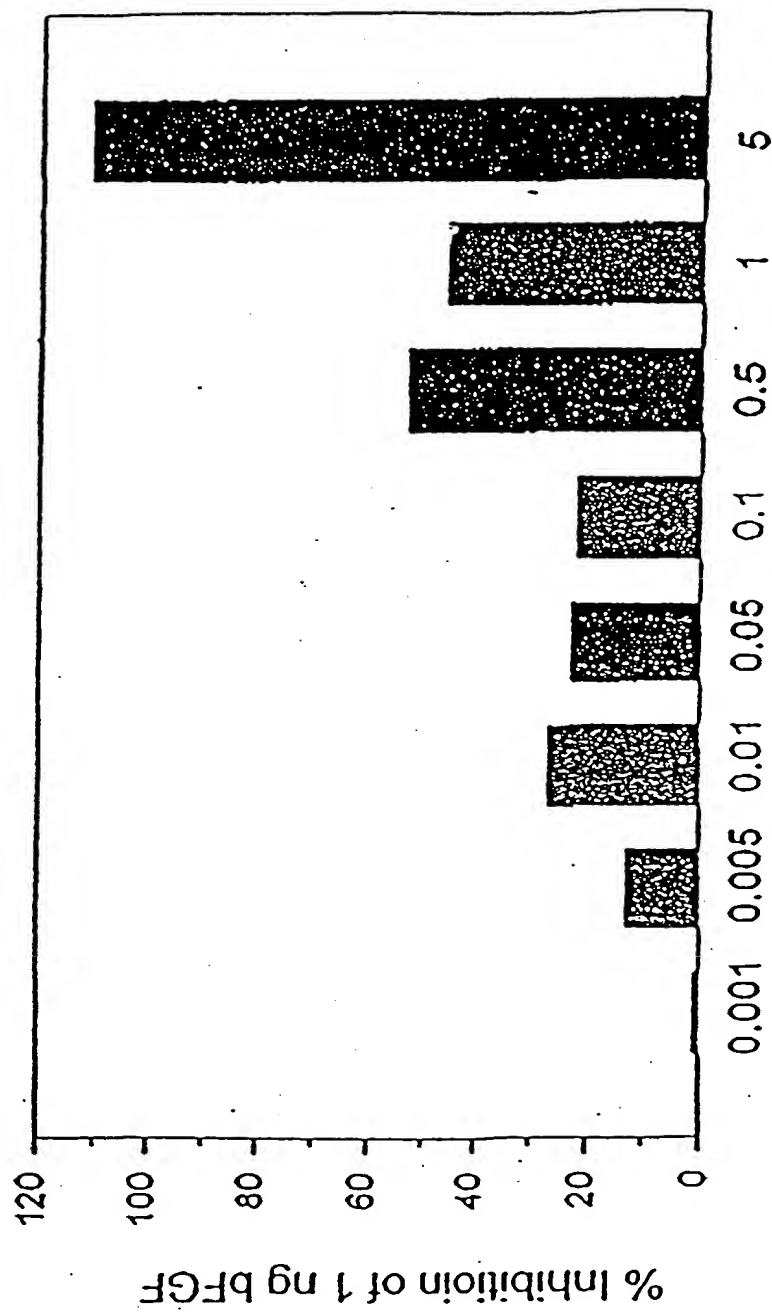


FIG. 4



UA-BRF-004-DELEP F035 $\mu\text{g/ml}$

FIG. 5

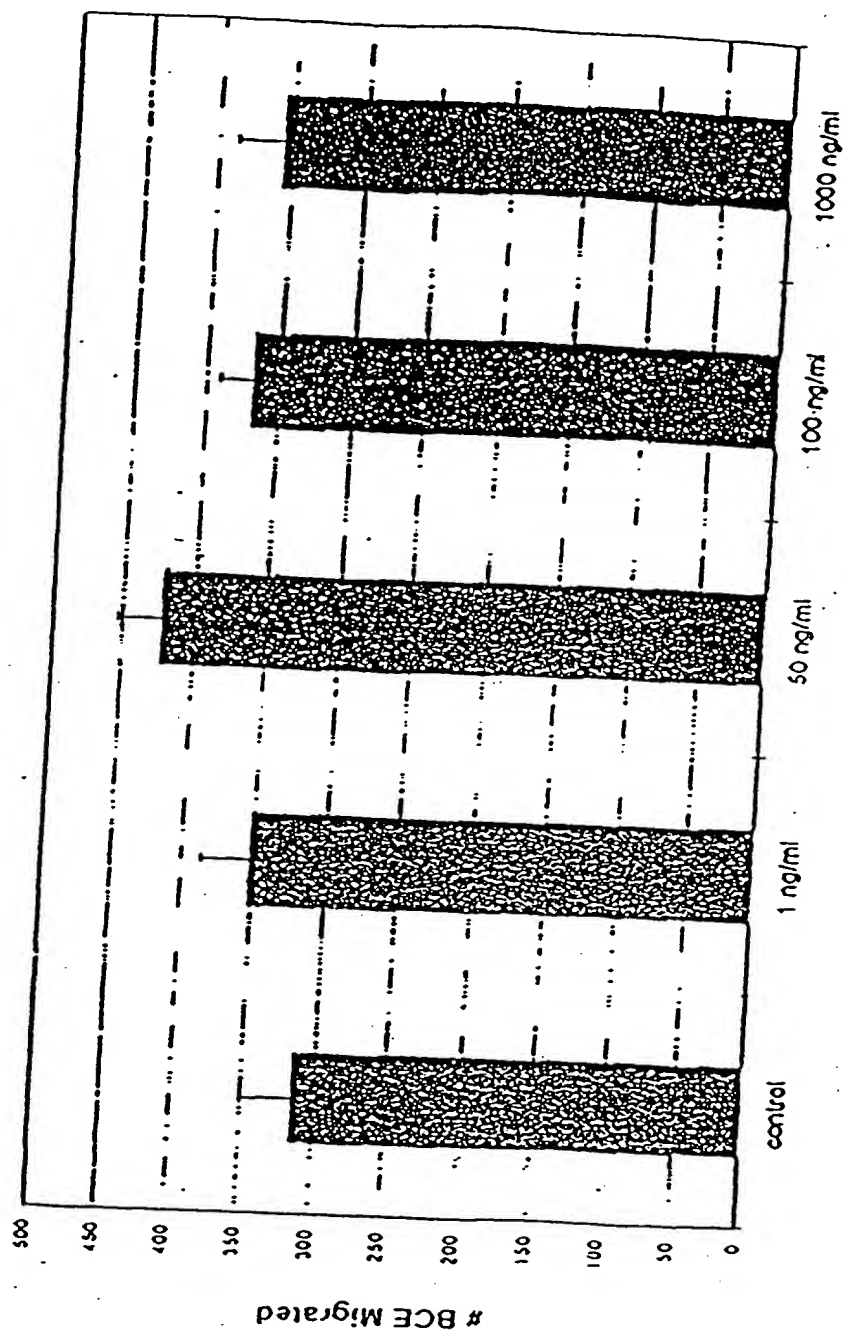


FIG. 6

TOP SECRET

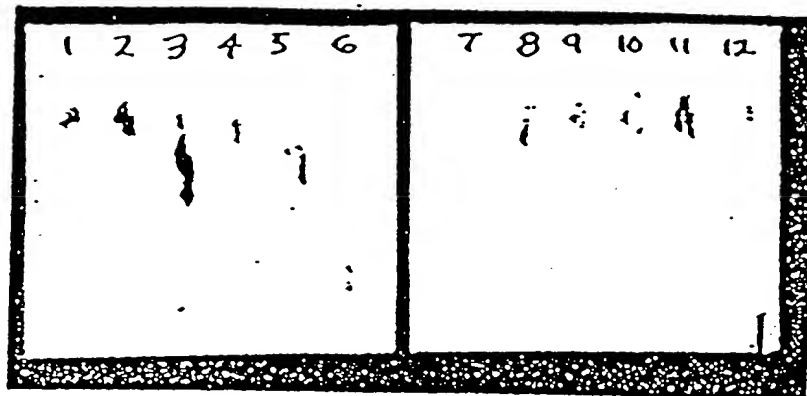


FIG. 7

FOOT " 932660



FIG. 8

Dose: 0.2 ml

ACETONE
4 weeks

Mouse # 133

FIG. 9A



Dose: 0.2 ml

ACETONE
8 Weeks

Mouse # 150

FIG. 9B



Dose: 100 nmol

DMBA
4 Weeks

Mouse # 120

FIG. 9C

Dose: 100 nmol

DMBA
8 Weeks

Mouse # 119

FIG. 9D

TOP SECRET

Dose: 0.3 mg

Compound # 35
4 weeks

Mouse # 136

FIG. 9E



Dose: 0.3 mg

Compound # 35 + DMBA
8 Weeks

Mouse # 140

FIG. 9F



Treatment (Low Conc.)

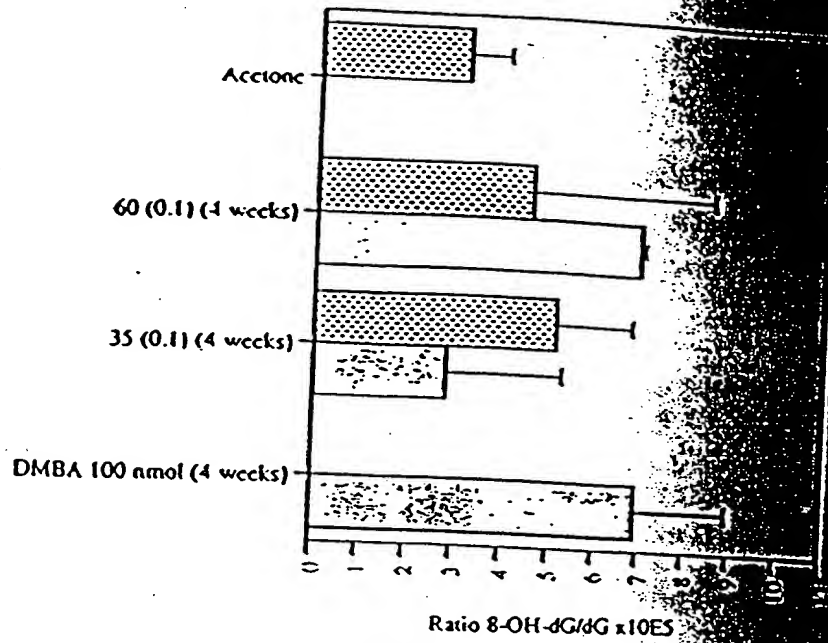


FIG. 10A

Treatment (High Conc.)

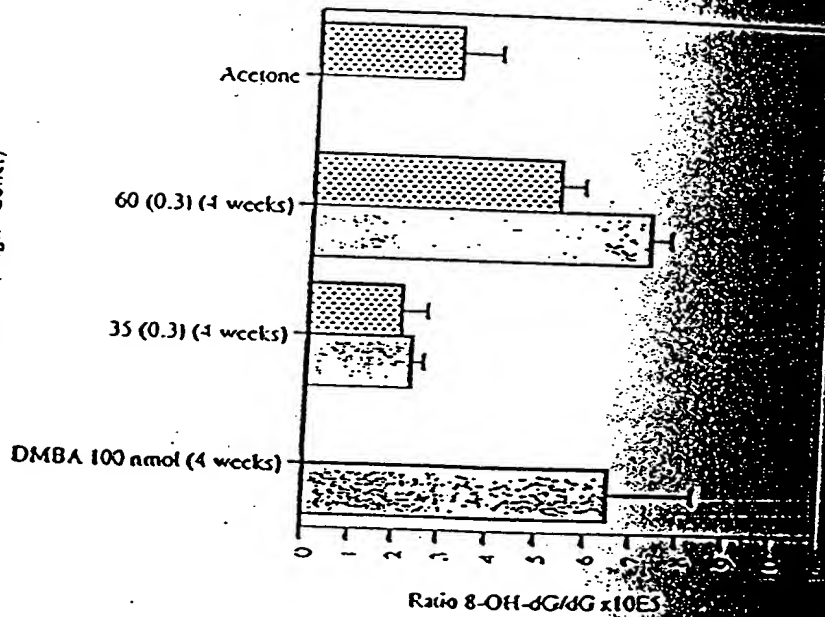


FIG. 10B

-DMBA
 +DMBA

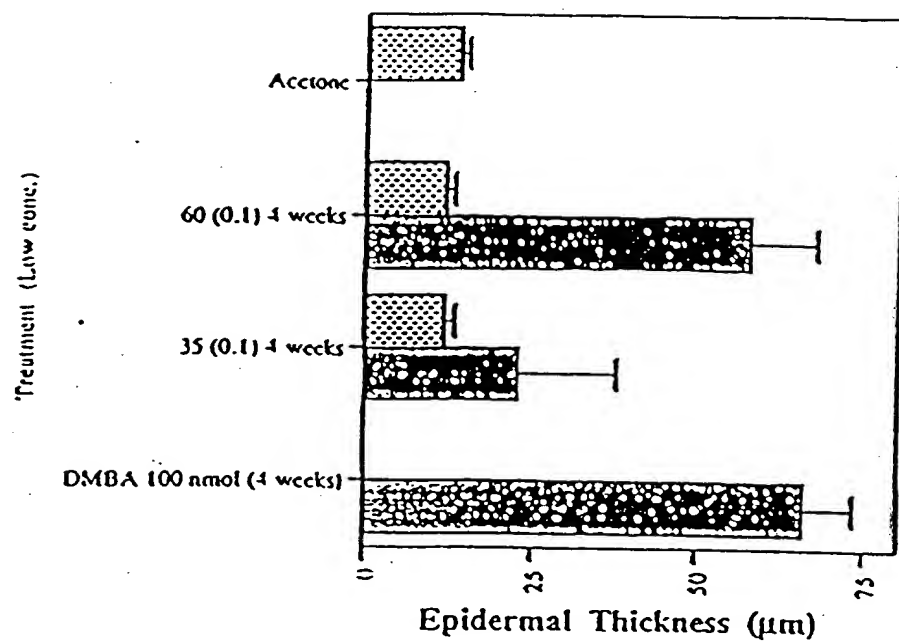


FIG. 11A

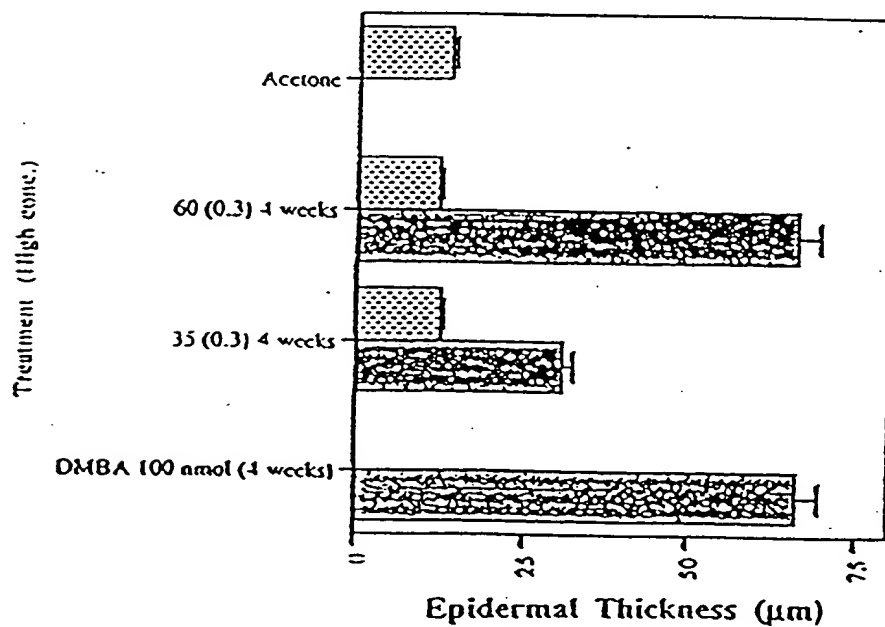


FIG. 11B

□ - DMBA
■ +DMBA

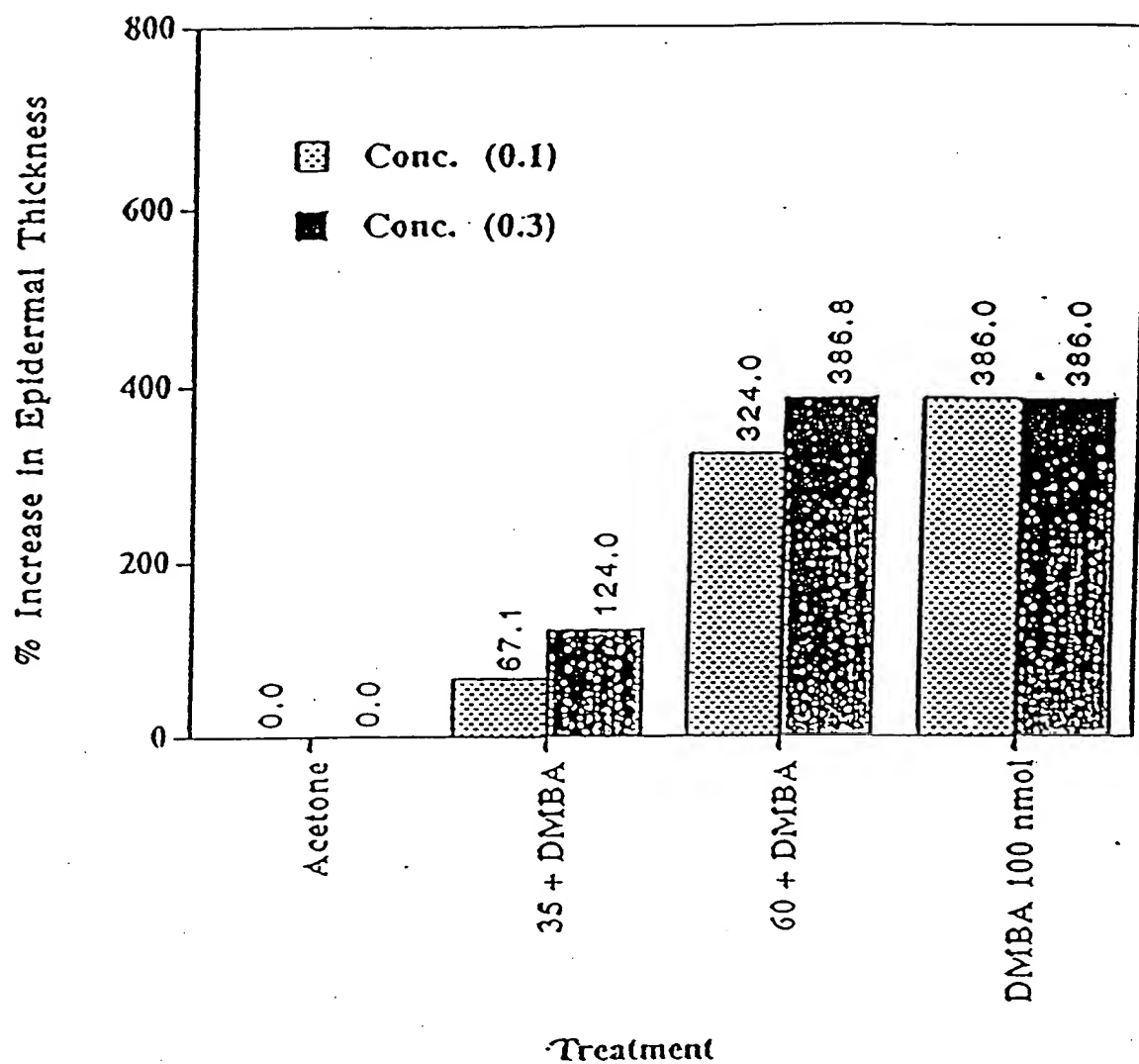


FIG. 12

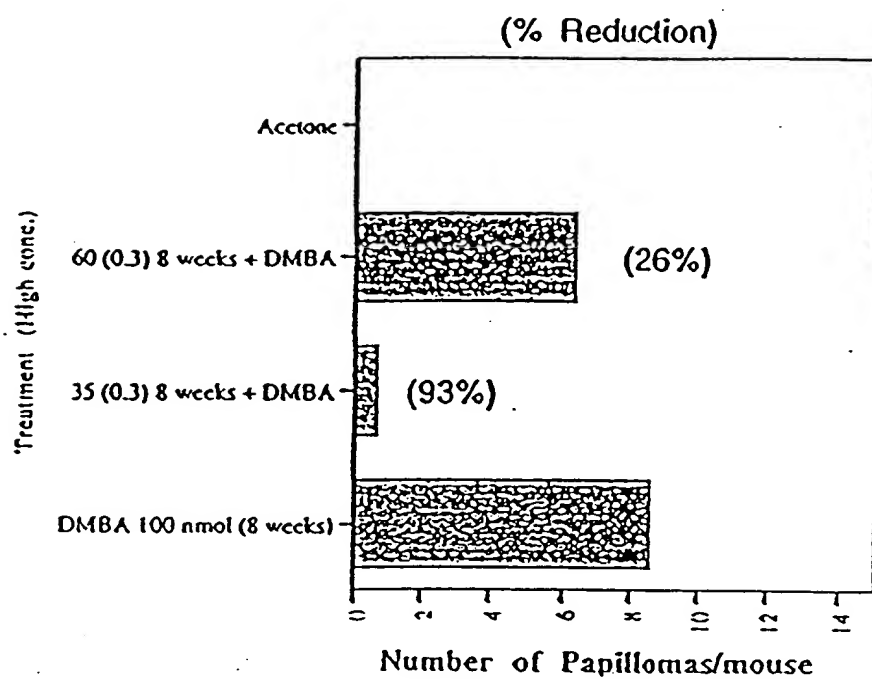


FIG. 13

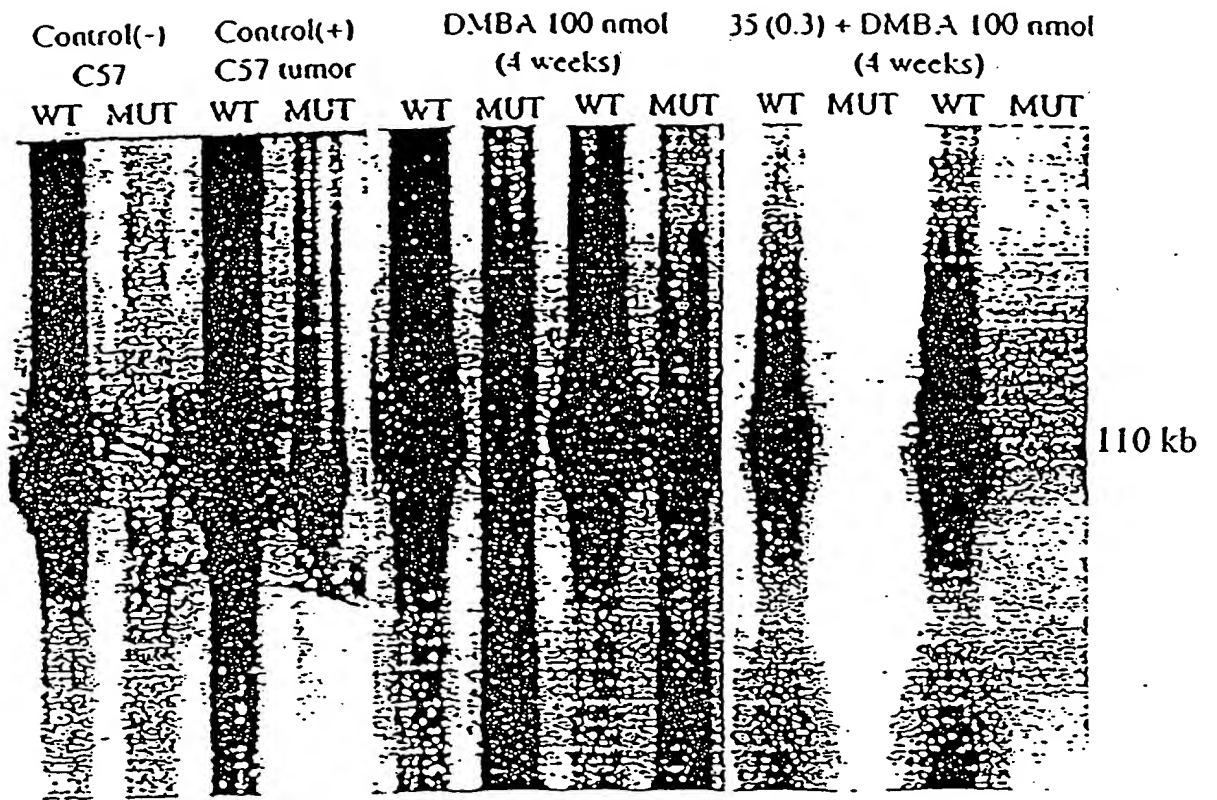


FIG. 14

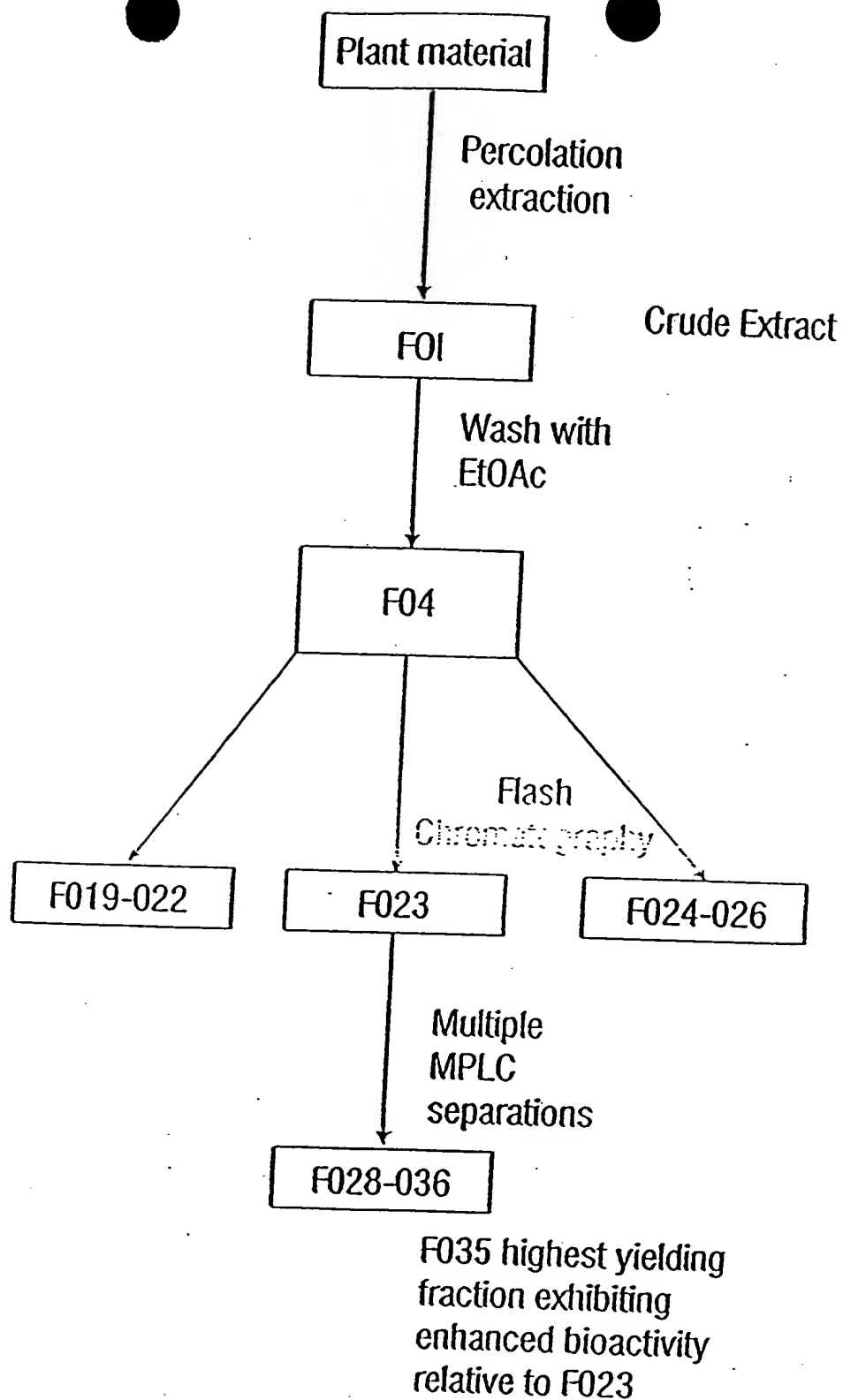


FIG. 15

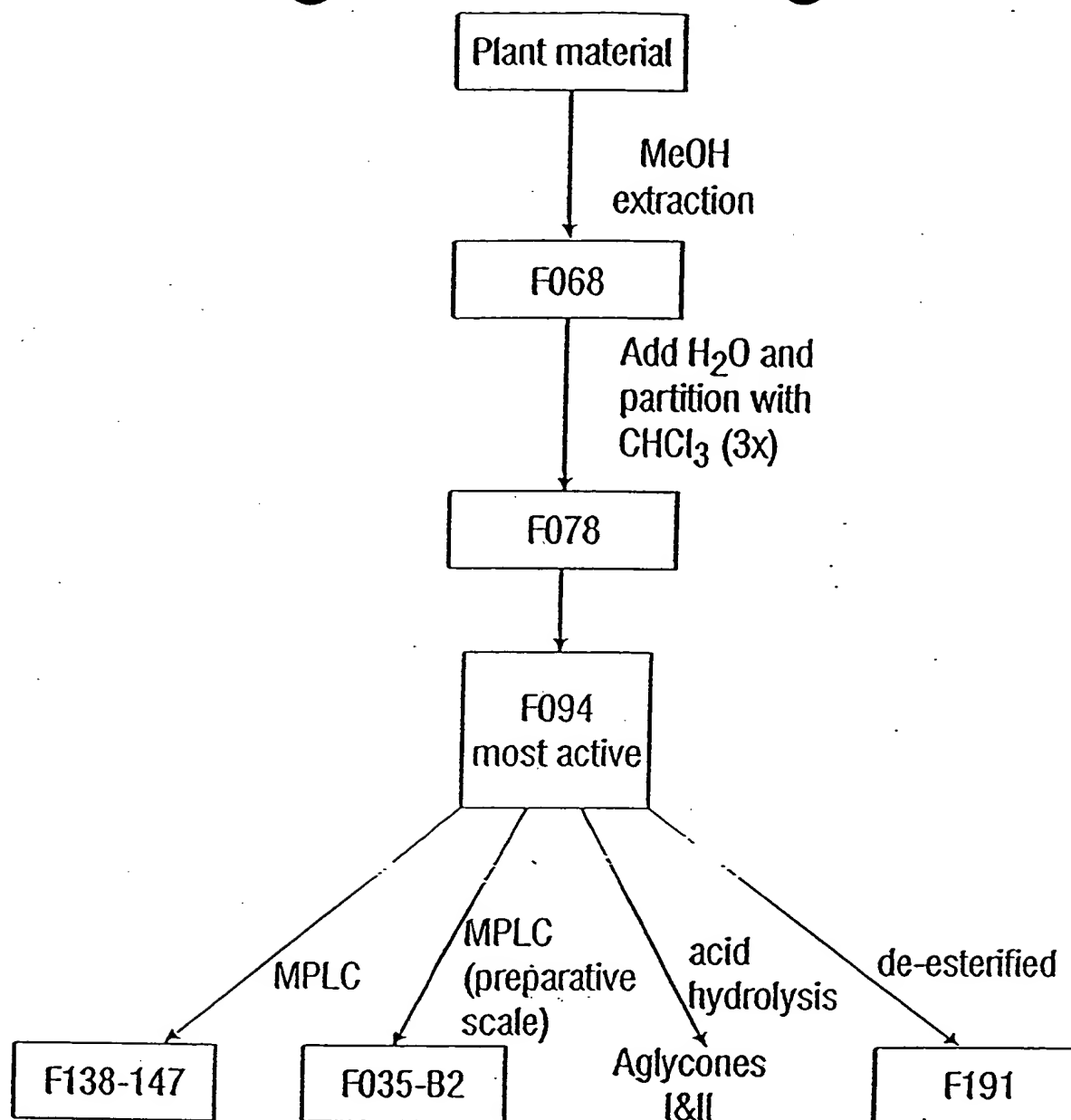


FIG. 16

iv



FIG. 17A

m
v

Figure 1

TEST 9552660

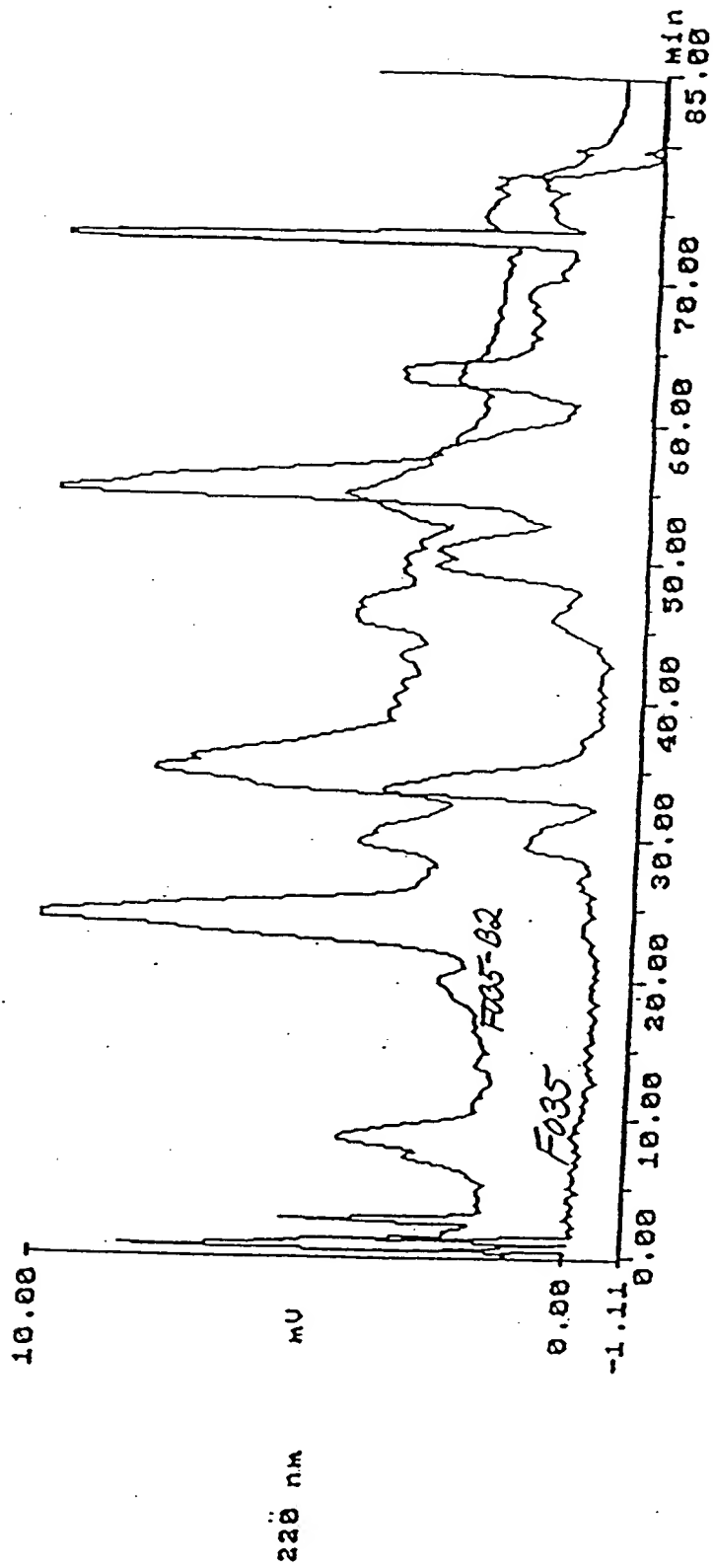


FIG. 18A

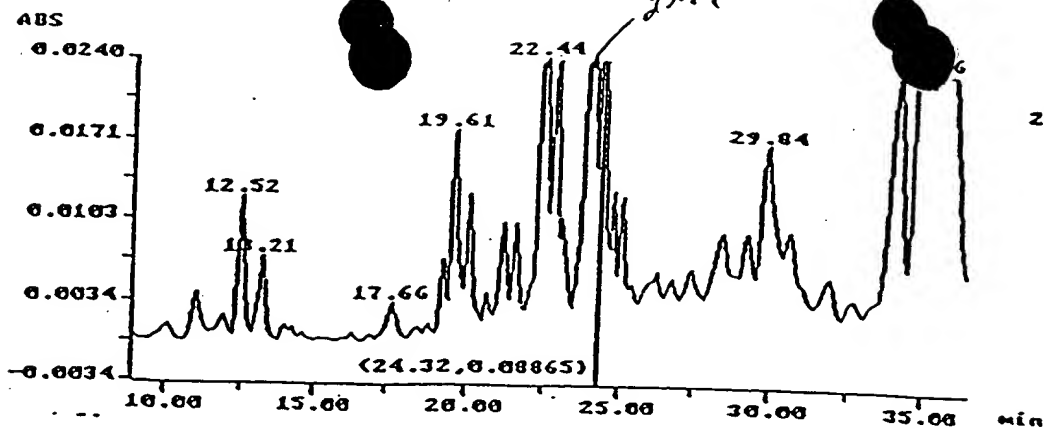


FIG. 18B

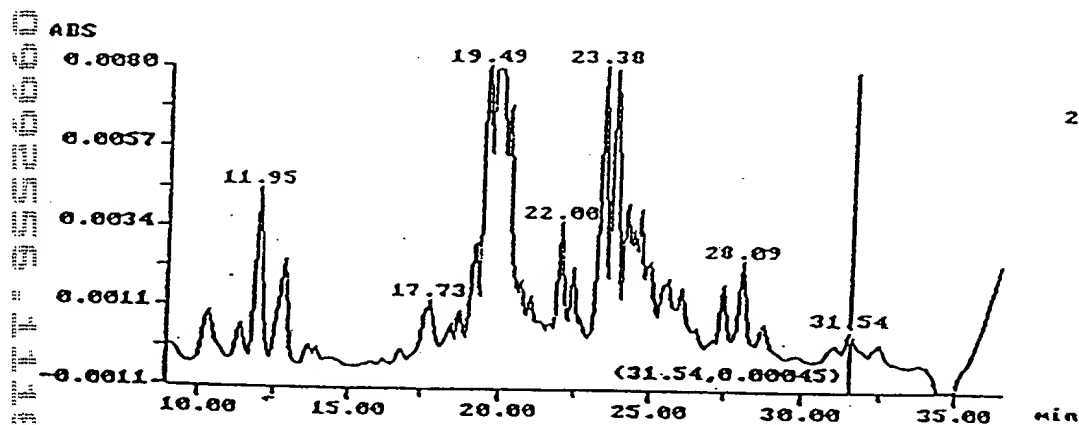


FIG. 18C

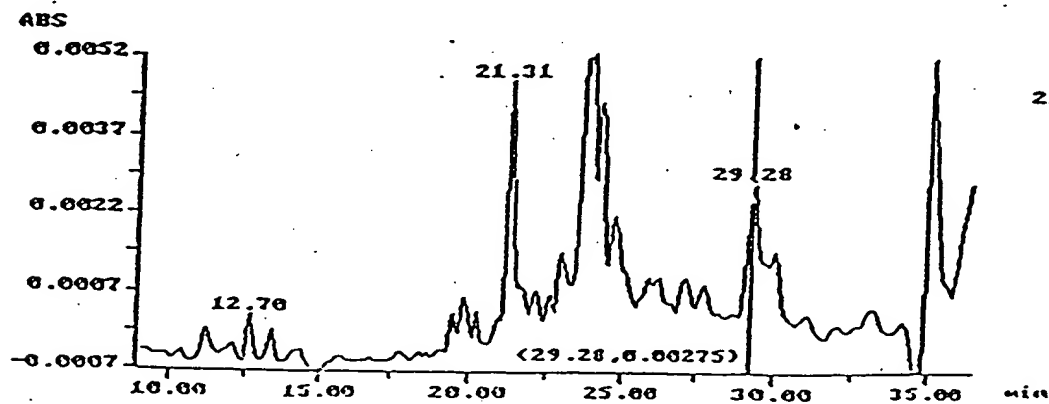


FIG. 18D

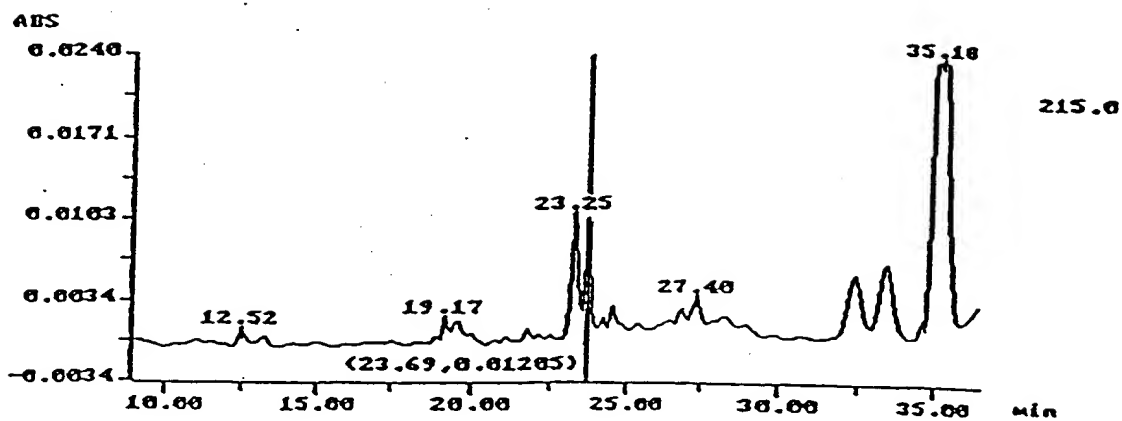


FIG. 18E

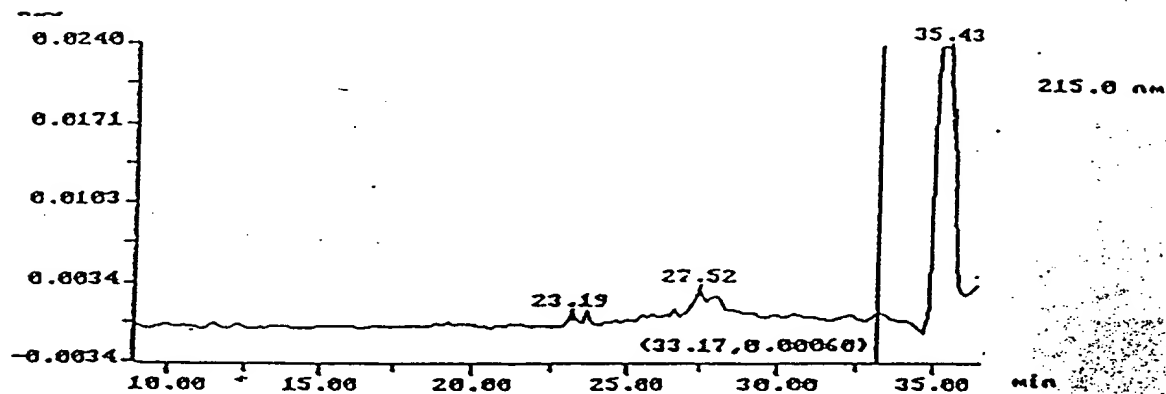


FIG. 18F

TEST: 952660

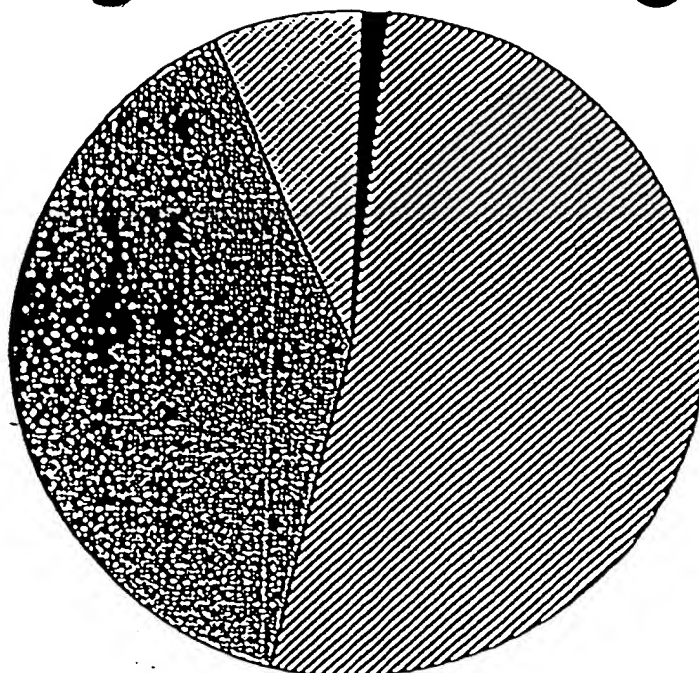


FIG. 19A

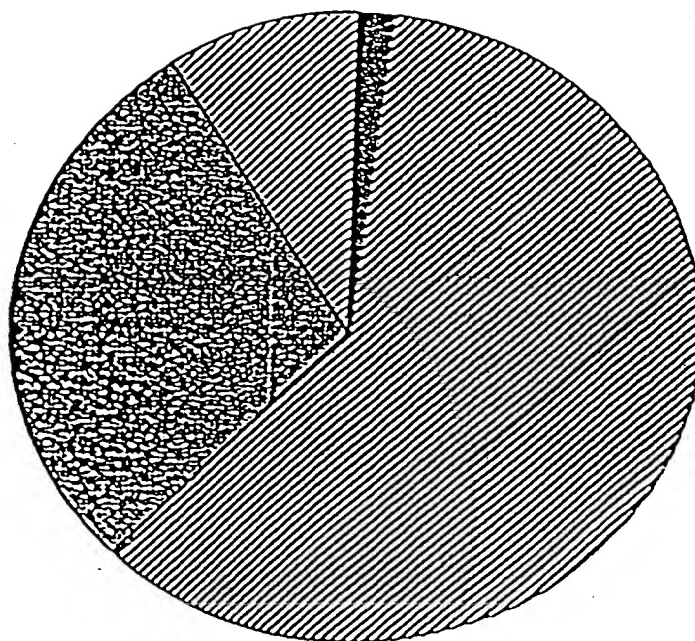
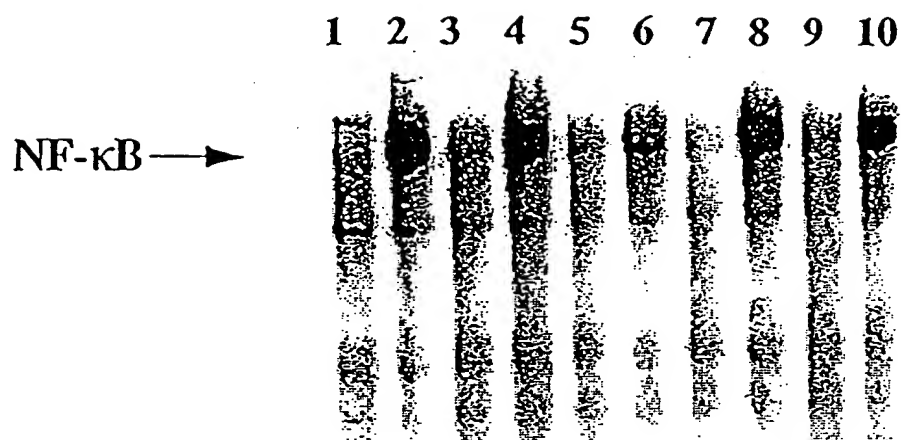


FIG. 19B



- 1 : Untreated
- 2 : TNF (100pM)
- 3 : F035 (1ug/ml)
- 4 : TNF+ F035 (1ug/ml)
- 5 : F035 (2μg/ml)
- 6 : TNF+ F035 (2μg/ml)
- 7 : F094 (1μg/ml)
- 8 : TNF+F094 (1μg/ml)
- 9 : F094 (2ug/ml)
- 10 : TNF+ F094 (2ug/ml)

FIG. 20






Time (h)	Fraction 35 treatment				Wort
	0	2	6	15	
					

FIG 21

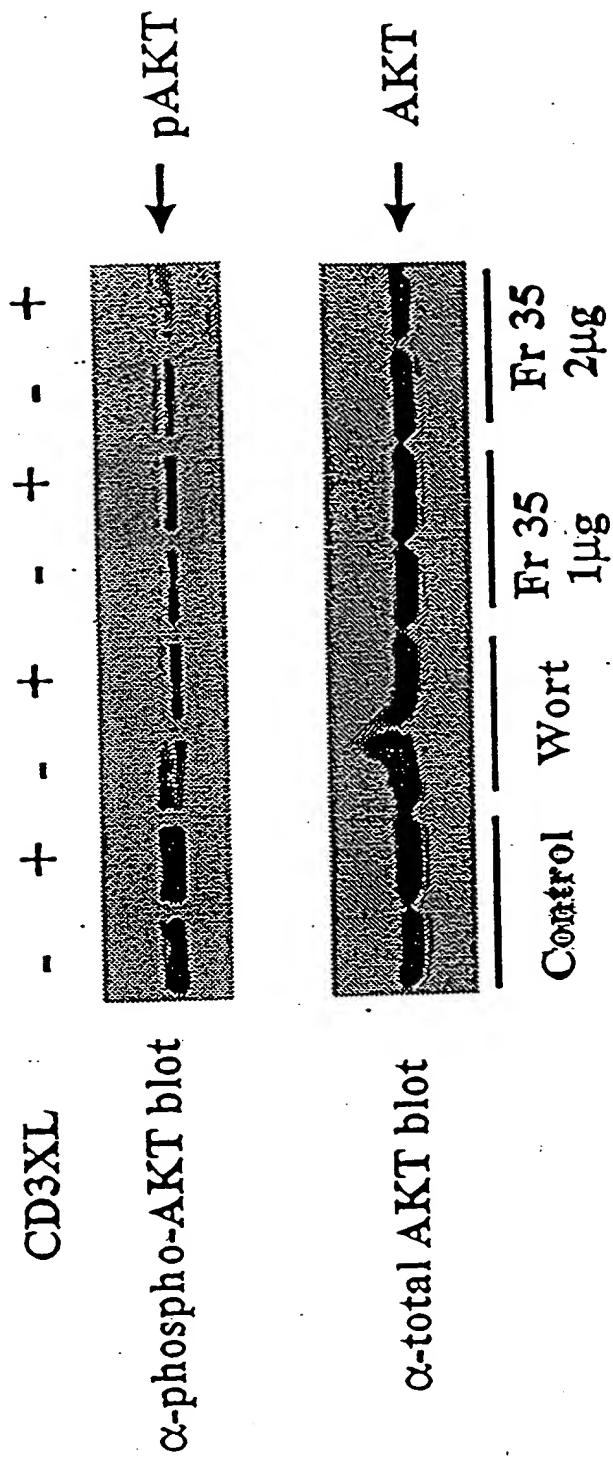


FIG 22

1

FIG 23

ELLIPTOSIDE E if $R=OH$

ELLIPTOSIDE A if R=H

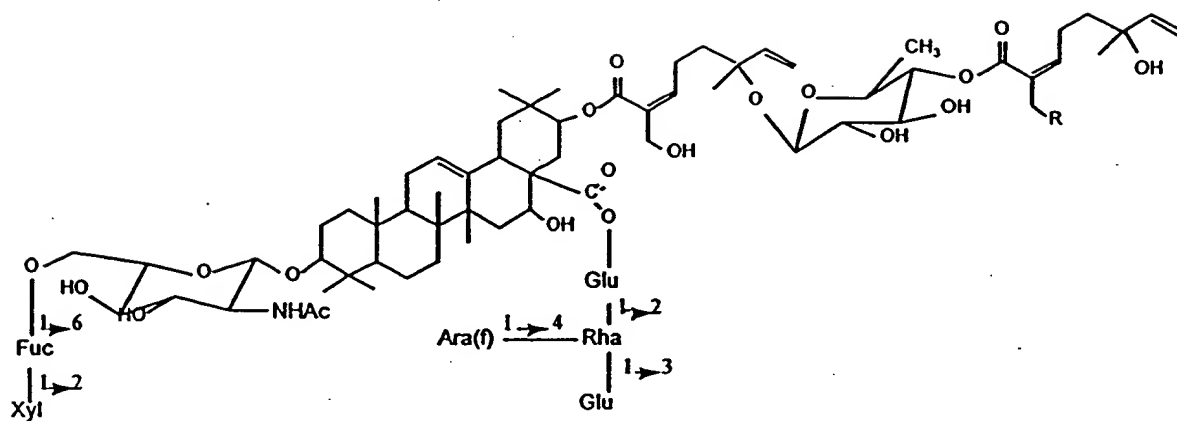


FIG 24

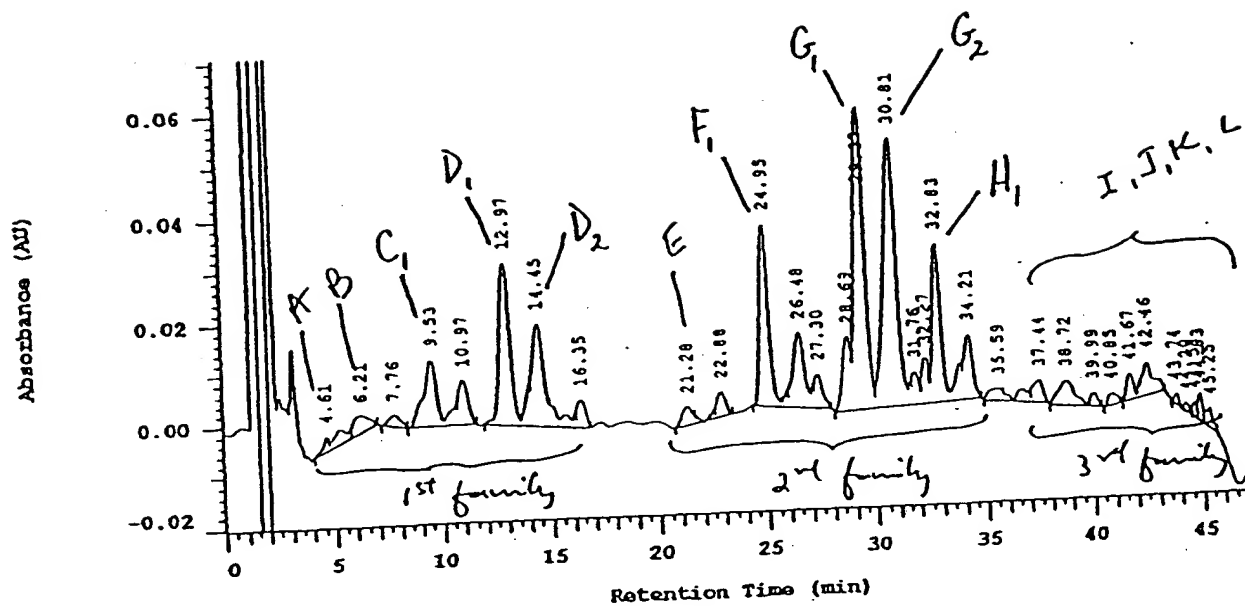
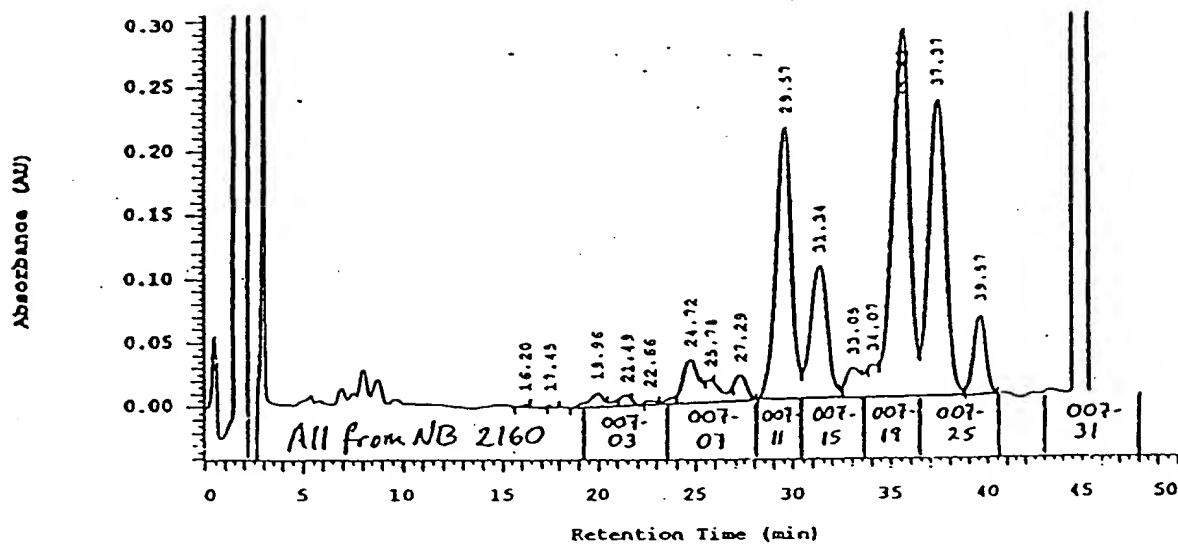


FIG 26

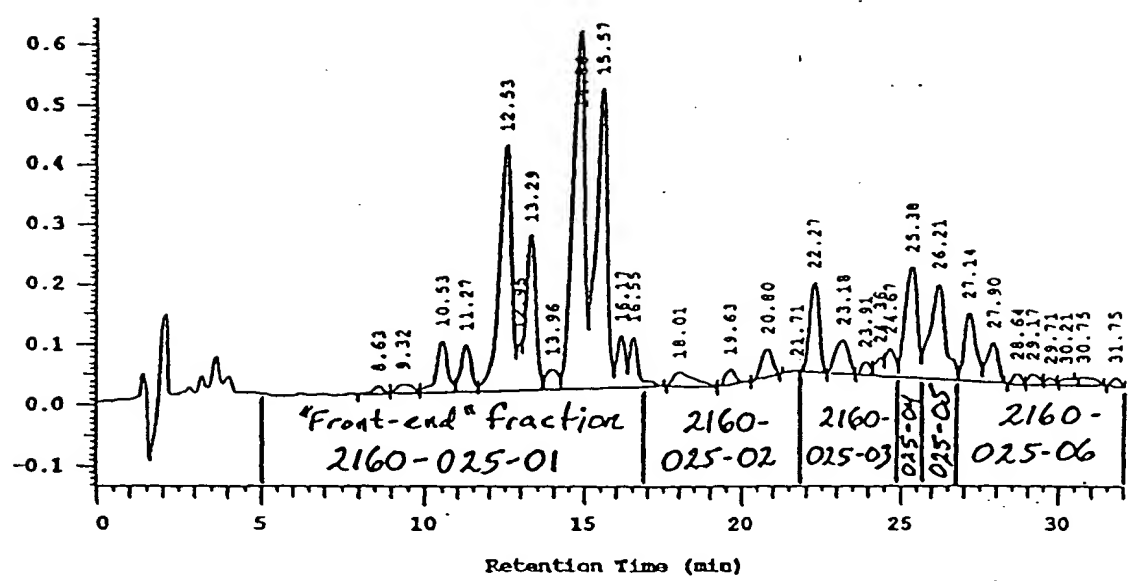
003T: 99999999



First Fractionation by Semi-Prep HPLC of F094

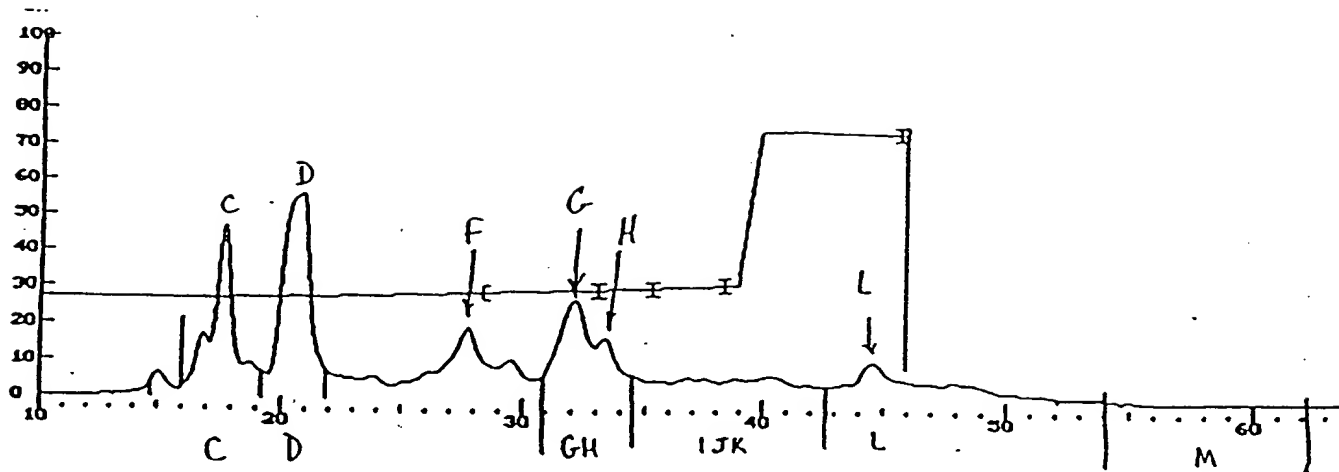
FIG 27

Absorbance (AU)



Second Fractionation by Semi-Prep HPLC of F094

FIG 28



Prep Fractionation of F094

FIG 29

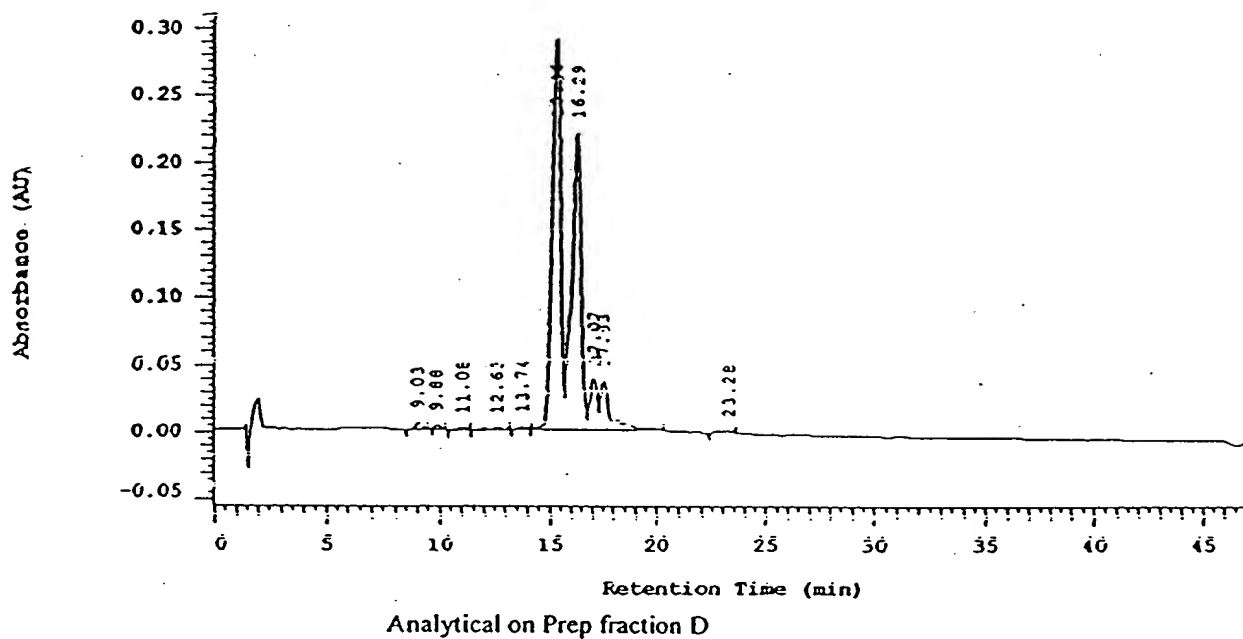


FIG 30

TEST: 956650

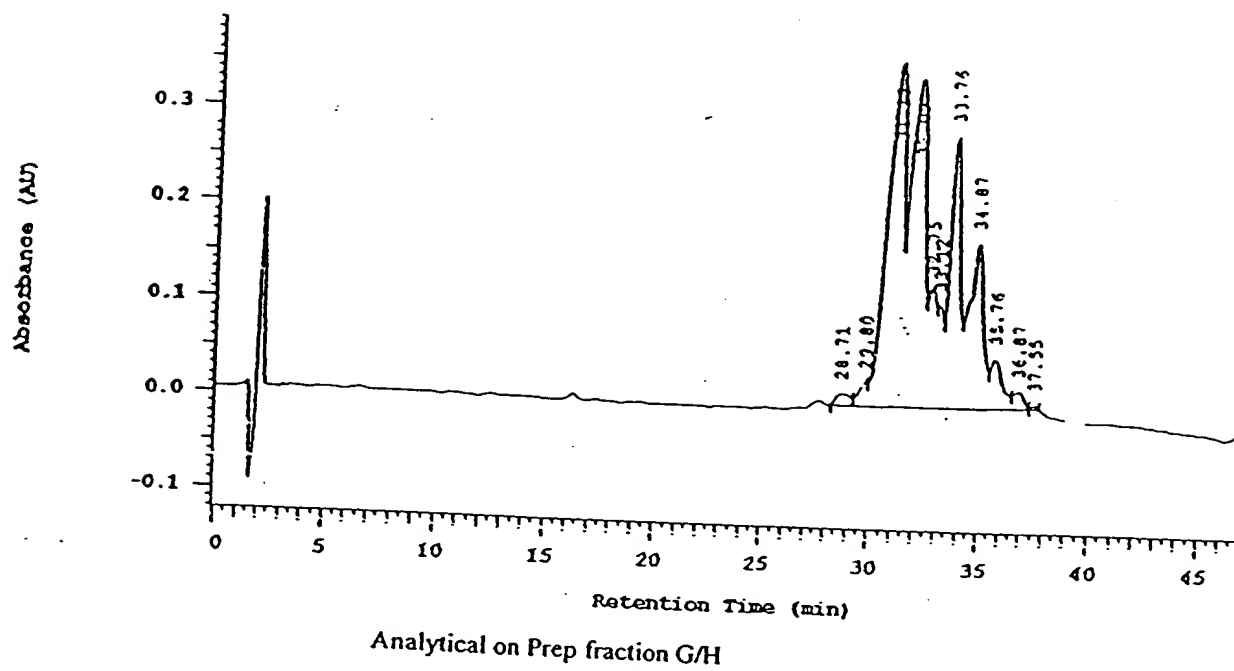
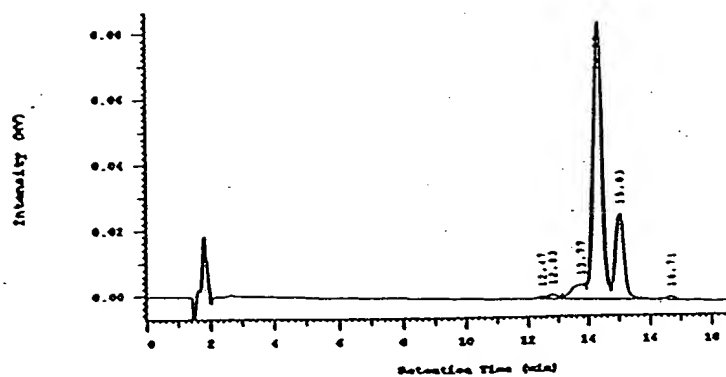


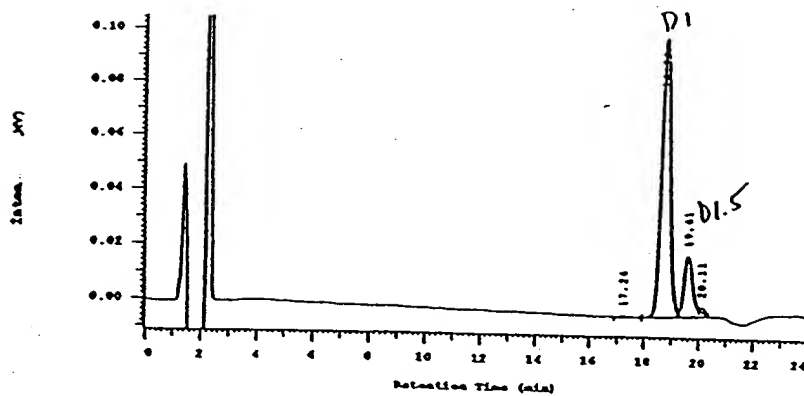
FIG 31



G1 after second PFP column purification.

FIG 32

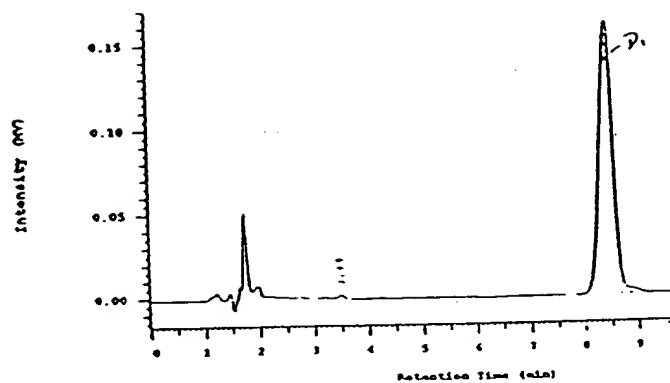
FIG 33



D1 after Waters C-18 column purification.

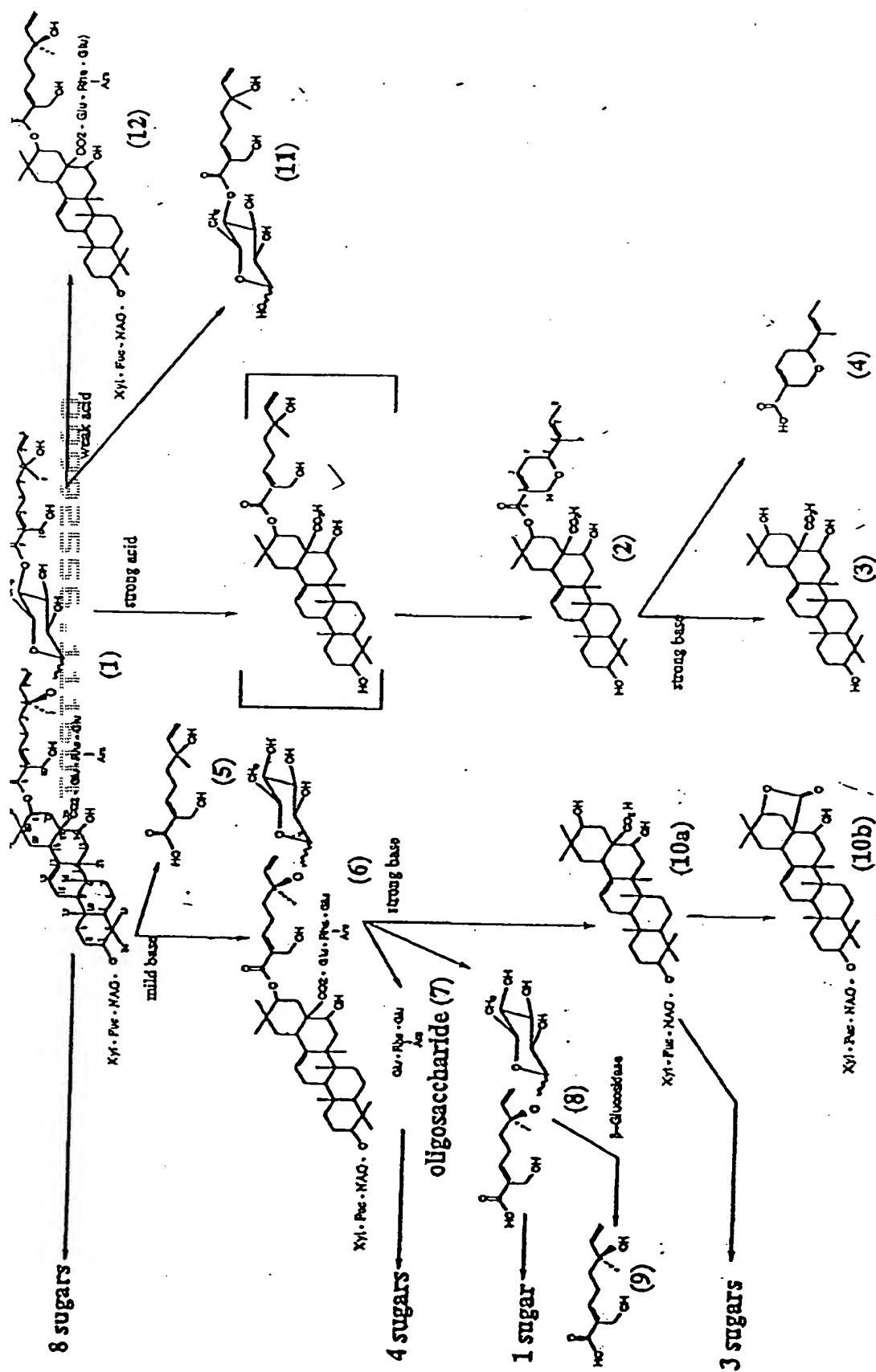
FIG 34

TOP SECRET



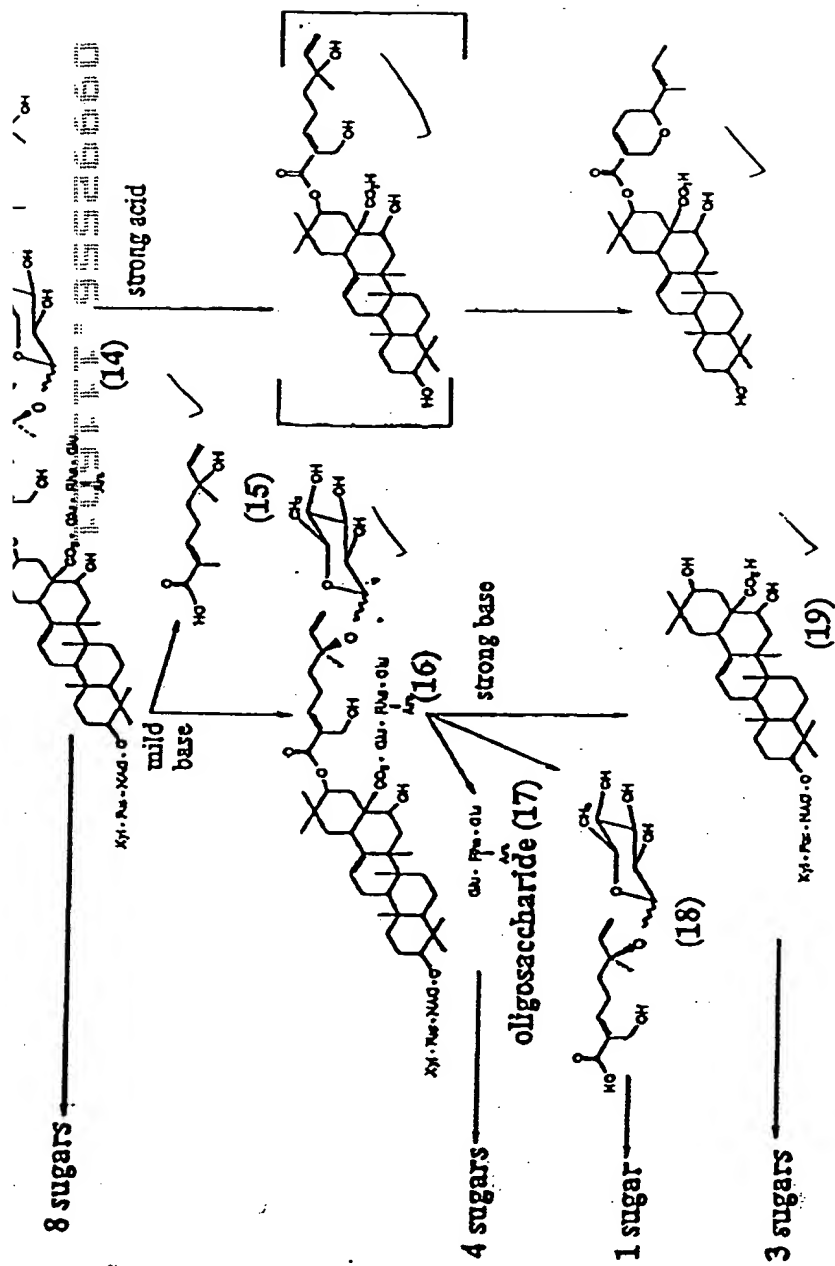
D1 after final C18-Aq purification

FIG 35



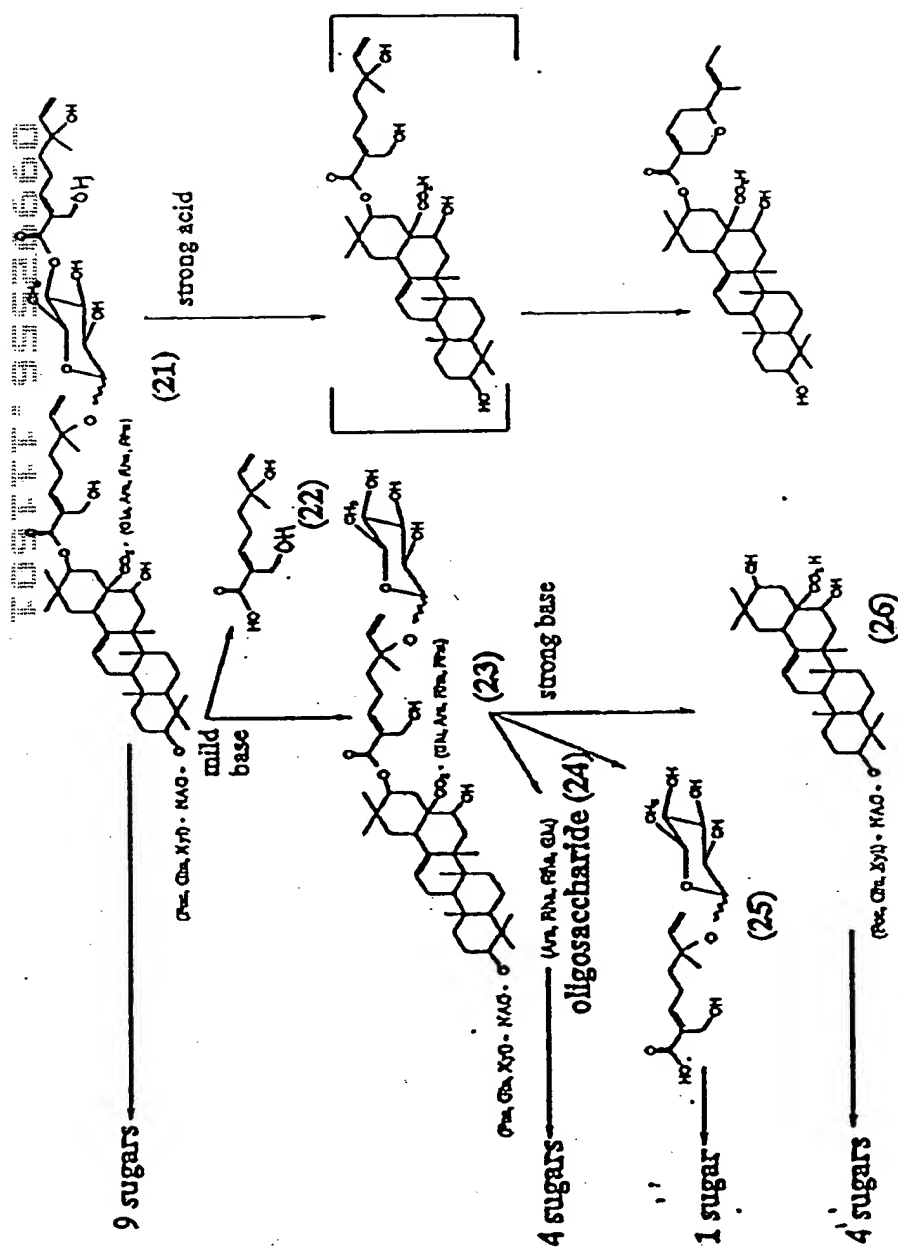
Compounds from the Degradation of D1

FIG 36



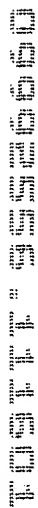
Compounds from the Degradation of G1

FIG. 37



Compounds from the Degradation of B1

FIG. 38



A: 209800()
A: 209800(#209800 v1 - C1.FR 00% Figures -Drawn by Priva)

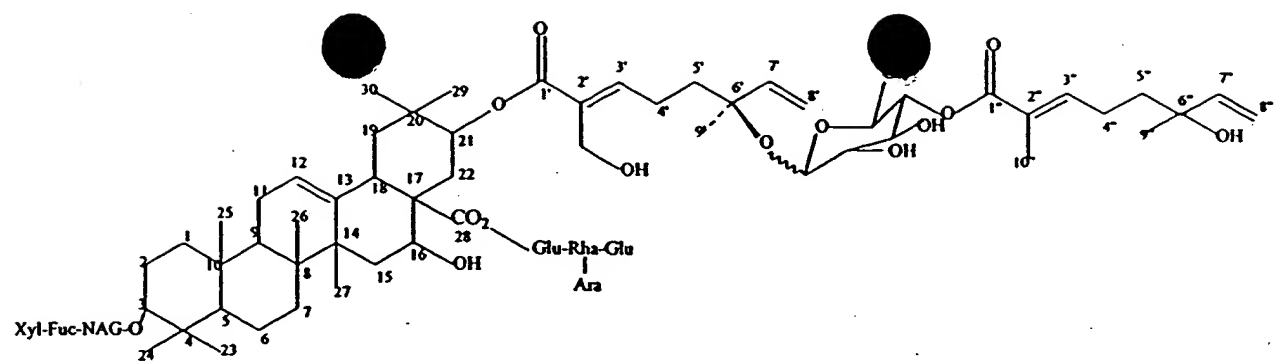


FIG. 40

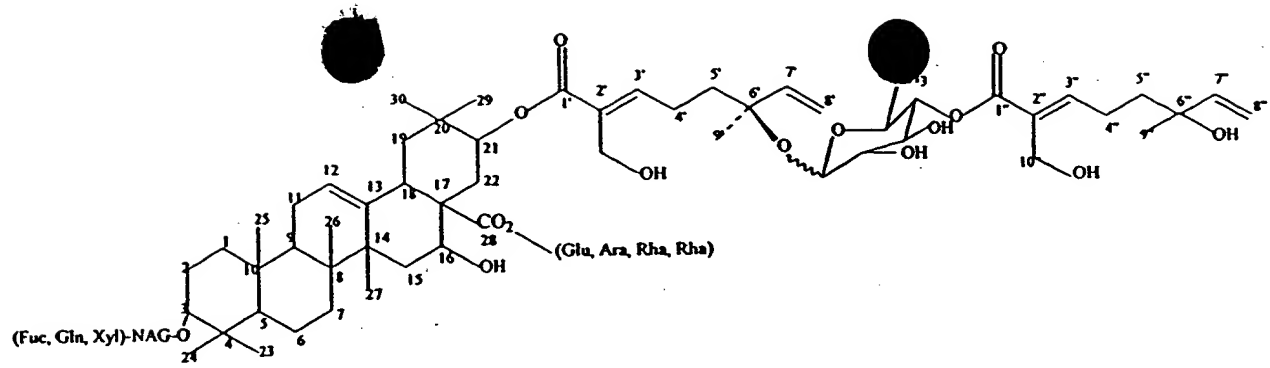


FIG. 41

Cell Line	IC ₅₀ (µg / ml)
MCF-10F (Normal Breast Epithelium)	> 25
MCF-10A (Normal Breast Epithelium)	> 25
L929 (Normal Mouse fibroblast)	> 25
Hs27 (Human foreskin fibroblast)	~14.5
MCF-7 (Breast)	> 25
BT-20 (Breast)	~14.5
SKBR-3 (Breast)	~12.5
MDA-468 (Breast)	~4.5
MDA-MB-231 (Breast)	~2.5
MDA-MB-435 (Breast)	~1.5
MDA-MB-453 (Breast)	~1.5
Lncap (Prostate)	~6.5
DU145 (Prostate)	~4.5
PC-3 (Prostate)	~2.5
PANC-1 (Pancreatic)	~2.5
A-498 (Renal)	~4.5
786-O (Renal)	~2.5
769-P (Renal)	~2.5
SKOV-3 (Ovarian)	~2.5
Dov-13 (Ovarian)	~2.5
C-2 (HEY VARIANT) (Ovarian)	~2.5
OVCAR-3 (Ovarian)	~2.5
JURKAT (T-cell leukemia)	~0.5

FIG. 42

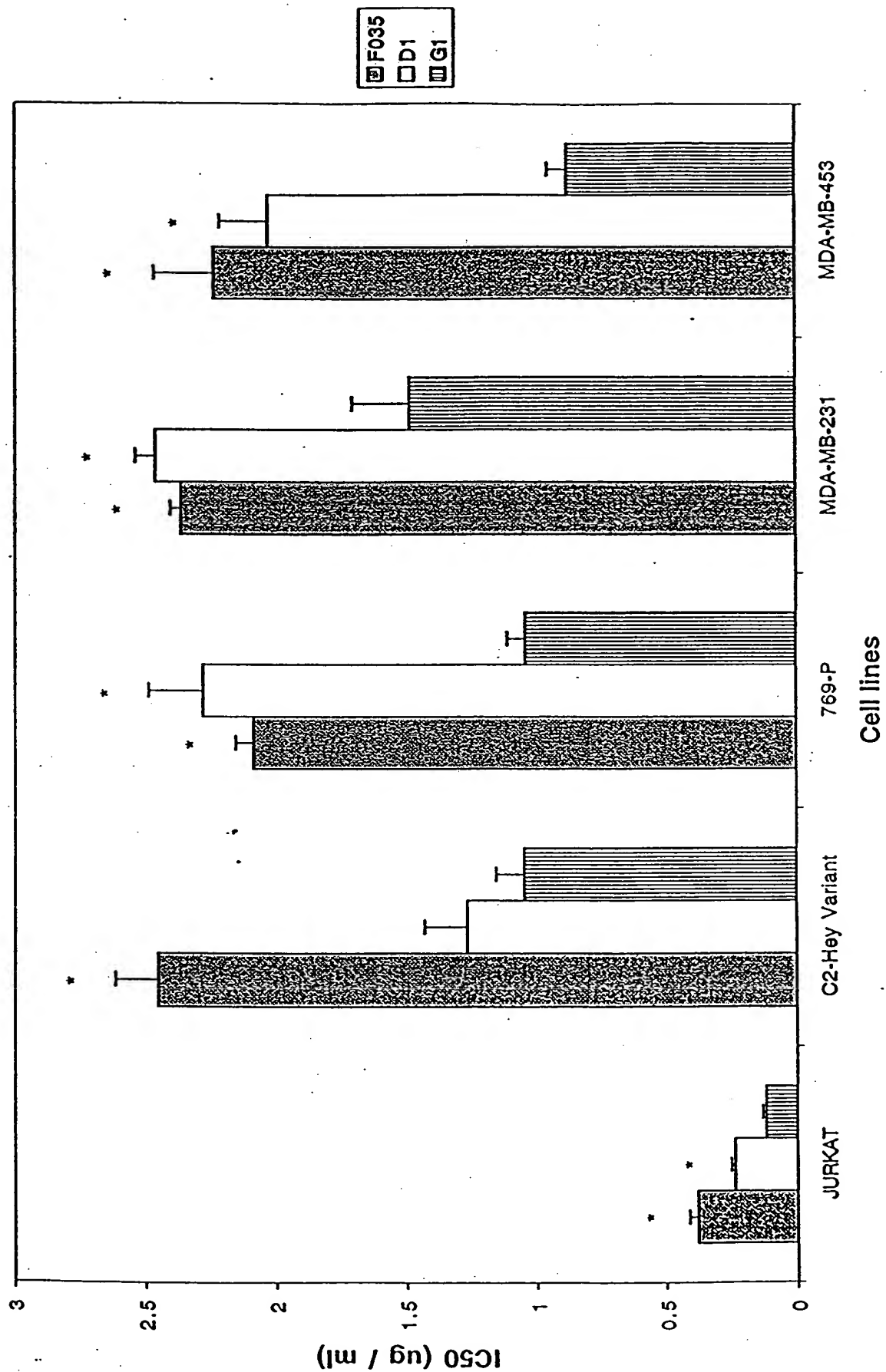
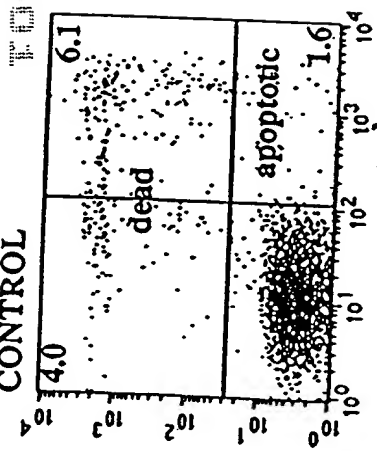
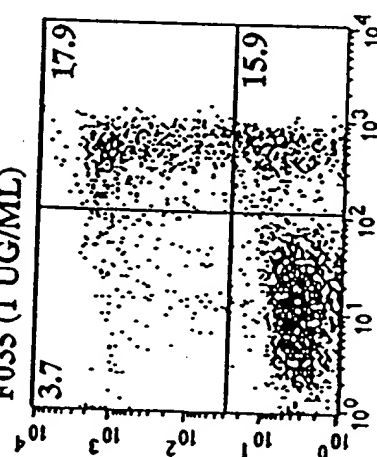


FIG 43

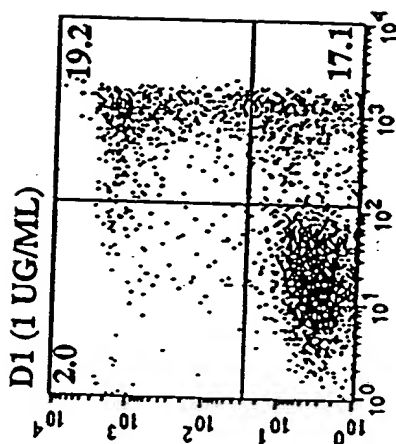
CONTROL



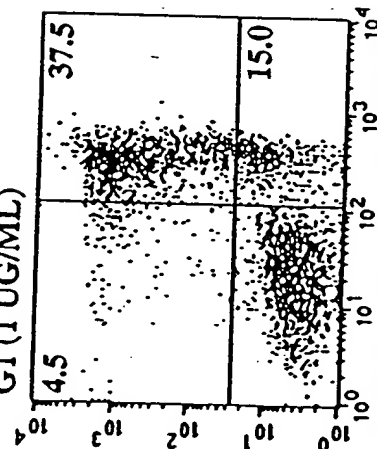
F035 (1 UG/ML)



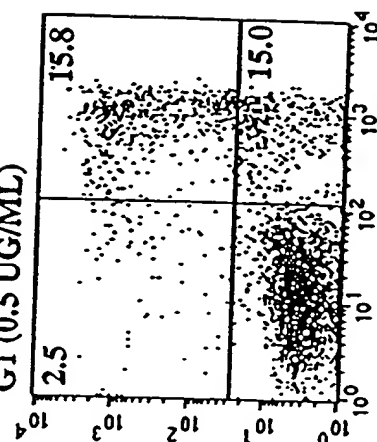
D1 (1 UG/ML)



G1 (1 UG/ML)



G1 (0.5 UG/ML)

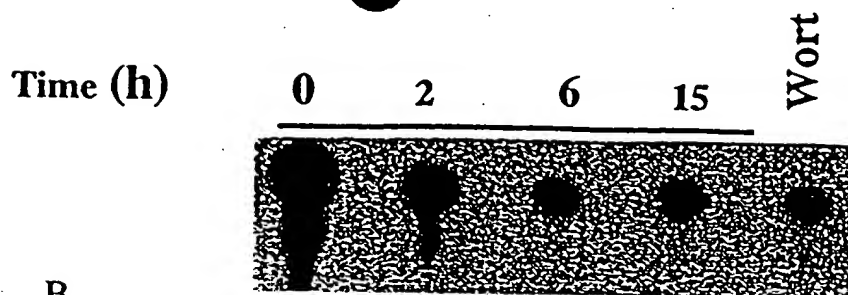


ANNEXIN-V-FITC

FIG 44

A

Forskolin 35 treatment



B

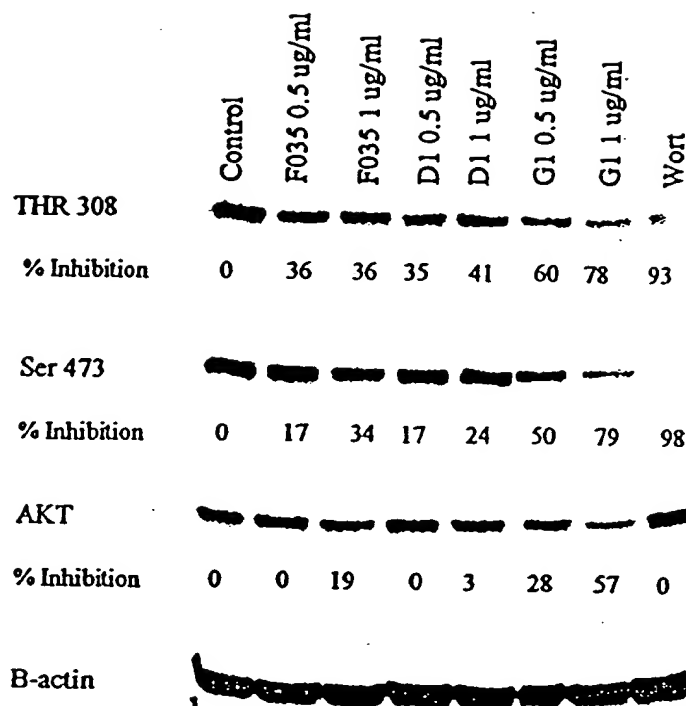


FIG 45

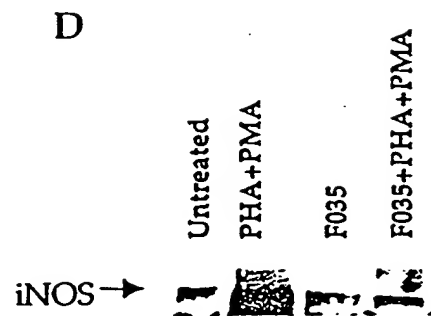
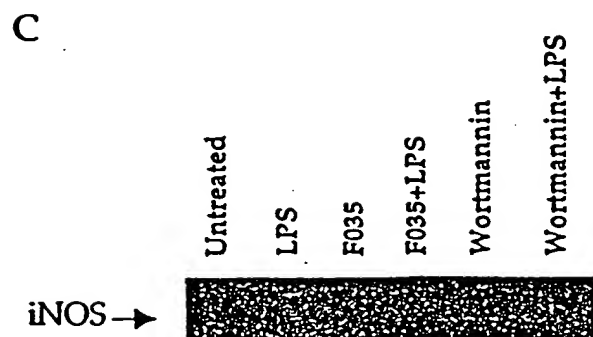
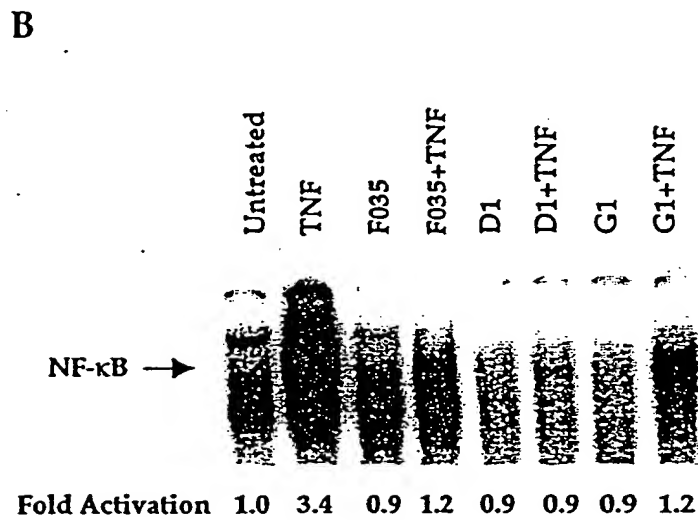
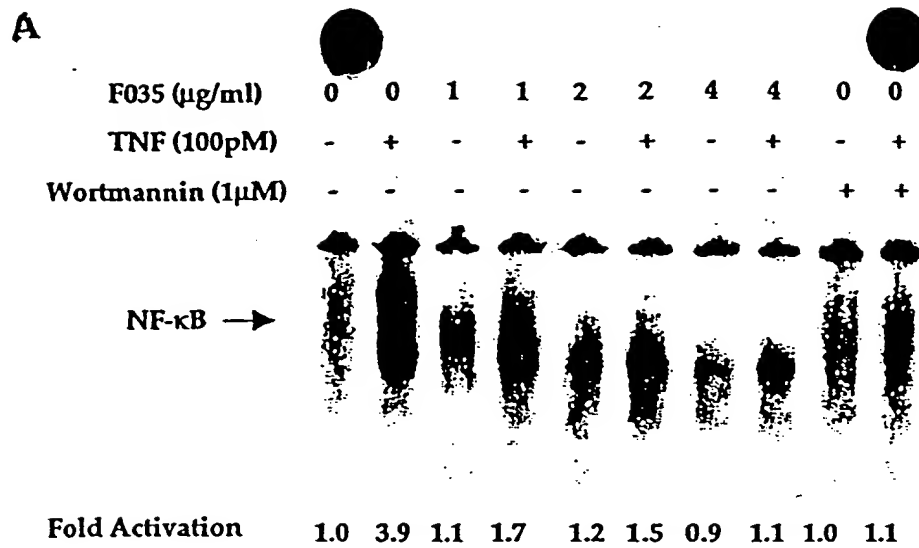


FIG 46

Effect of F035 & D1 on cleavage of PARP in Jurkat cells.

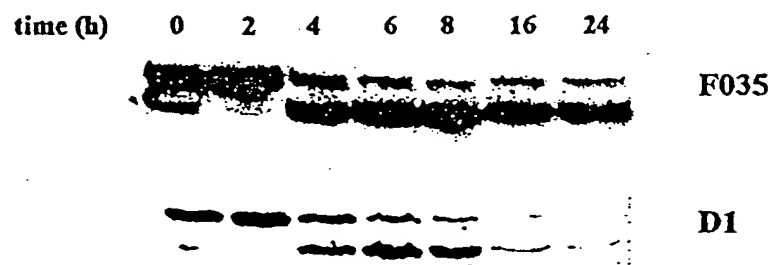


FIG 47

Effect of z-vad fmk on F035 induced PARP cleavage in Jurkat cells

F035	-	+	-	+
z-vad fmk	-	-	+	+

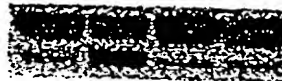


FIG 48

Effect of F035, F094, D1 & G1 on caspase activity in Jurkat cells.

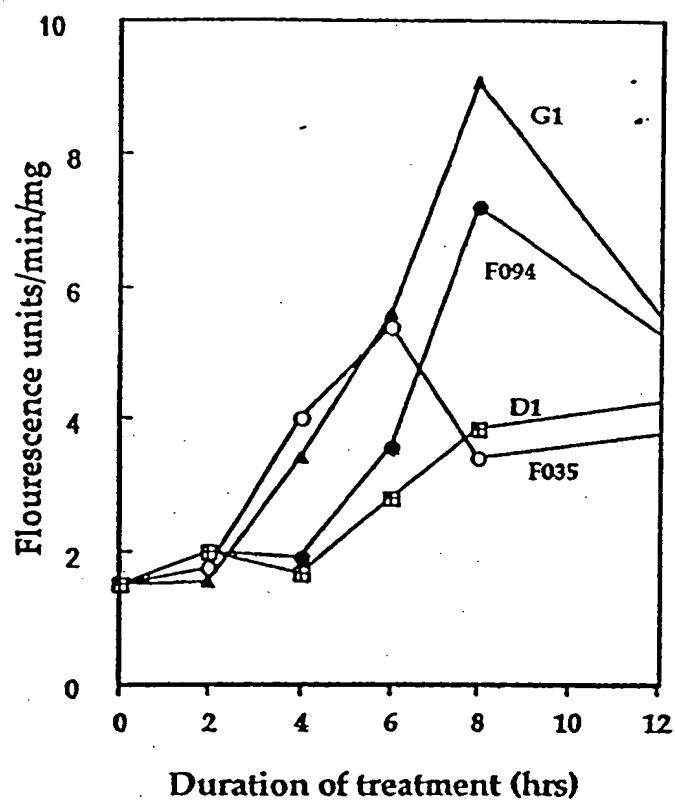


FIG 49

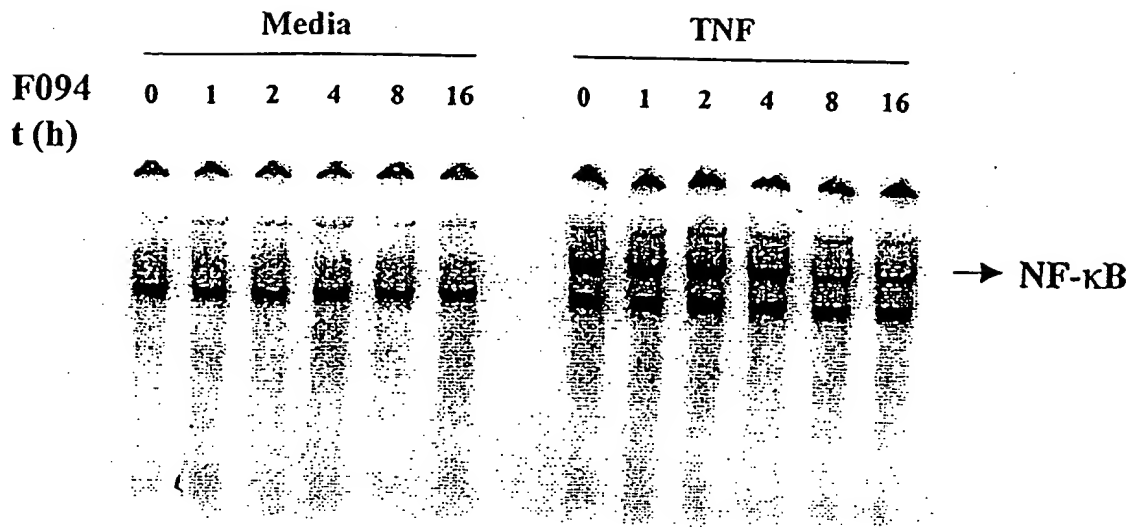
Effect of F035 on cytochrome c release from Jurkat mitochondria

time (h) 0 4 6
 → Cytochrome c

FIG 50

FOST-9552660

A



B

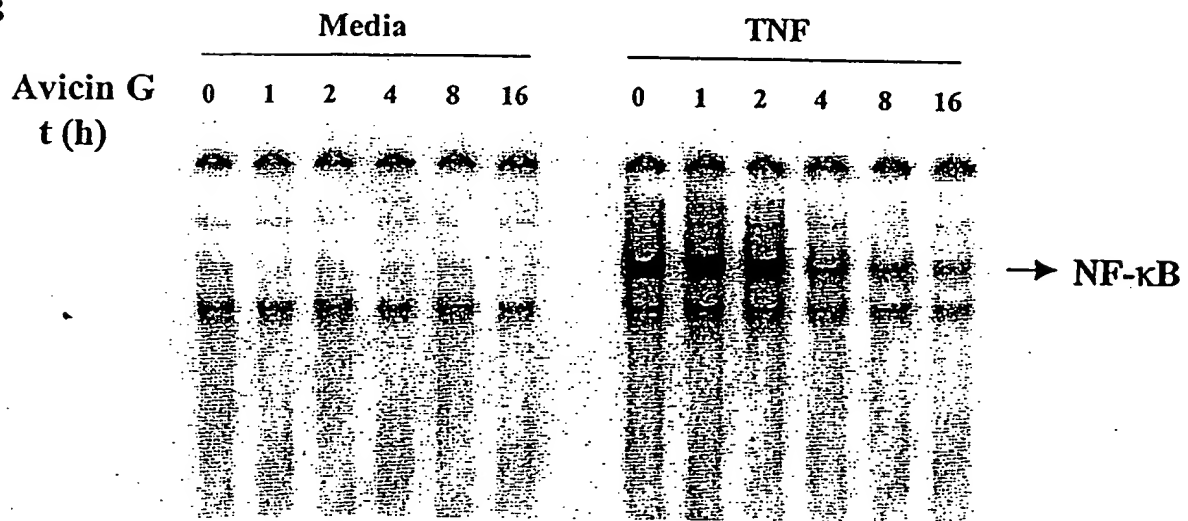
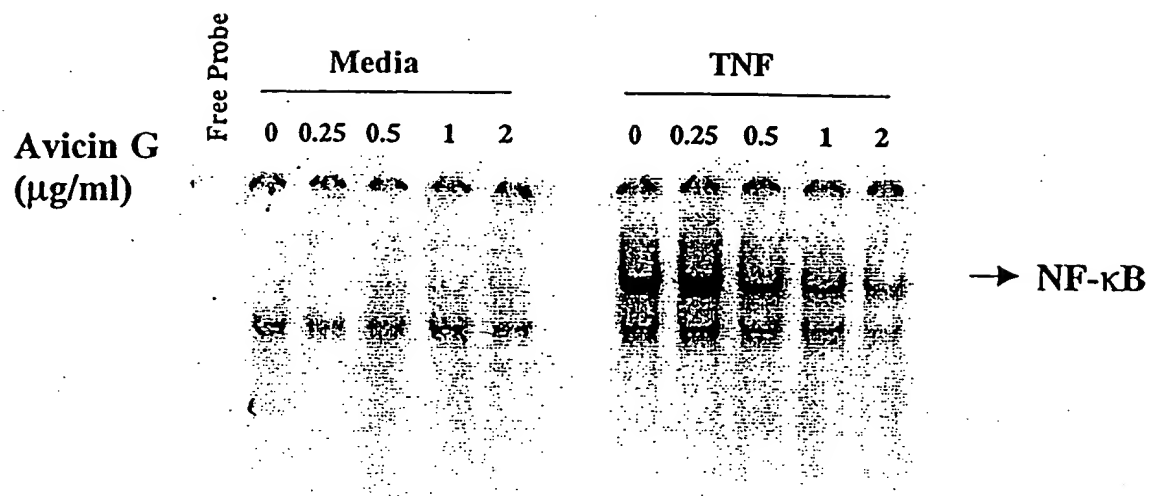


FIG. 51 A-B

A



B

Rabbit IgG	-	-	-	-	-	+
anti-p65	-	-	-	-	+	-
Cold wt	-	-	-	+	-	-
Cold mut	-	-	+	-	-	-
TNF	-	+	+	+	+	+

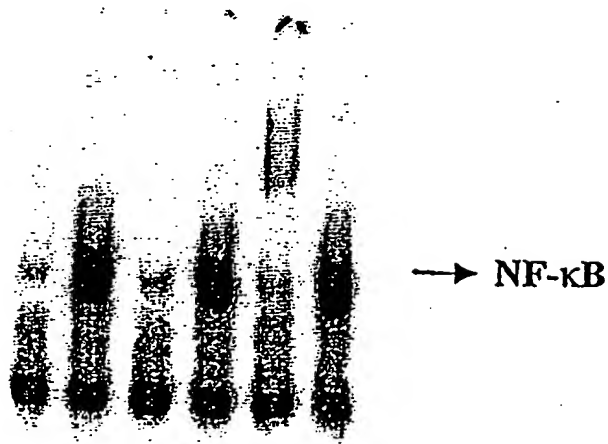
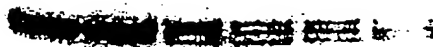


FIG. 52 A-B

FOST-959660

A **I κ B**

Time (min) 0 2 5 10 15 30



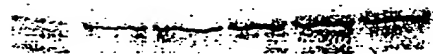
Untreated



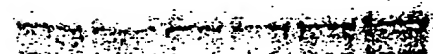
Avicin G

B **p65**

Time (min) 0 2 5 10 15 30



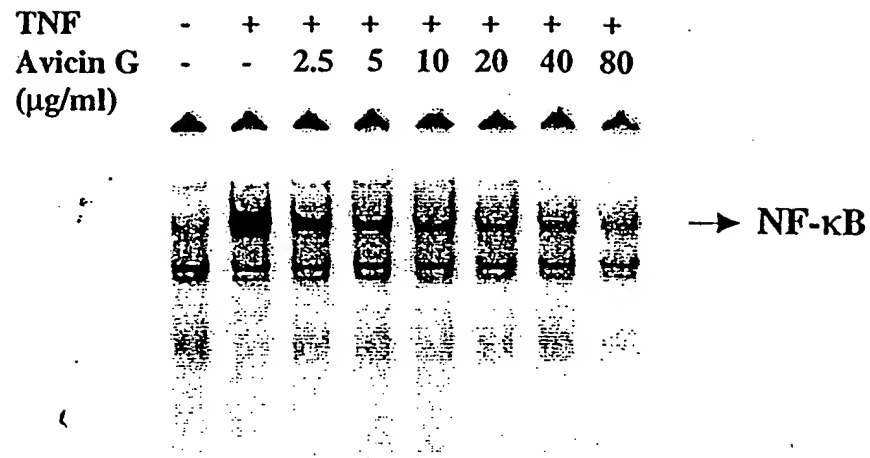
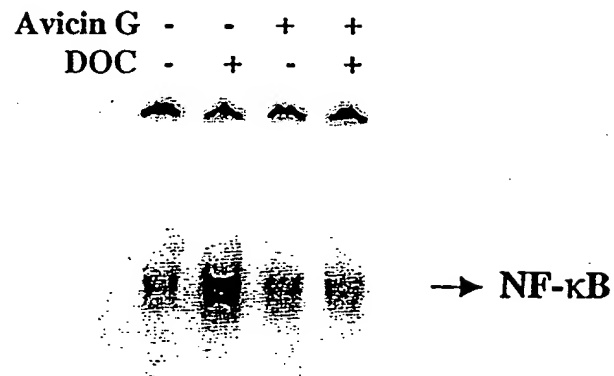
Untreated



Avicin G

FIG. 53 A-B

A

**B**

C

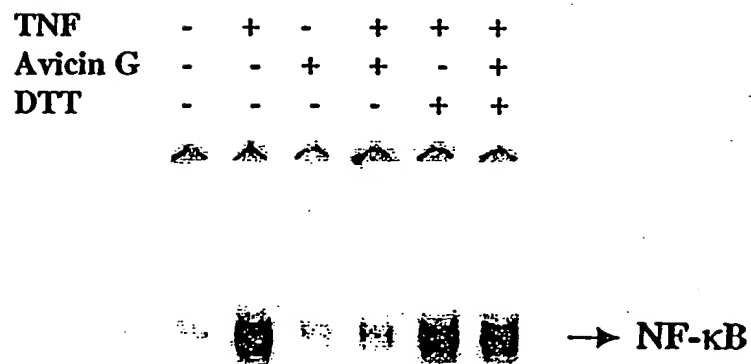
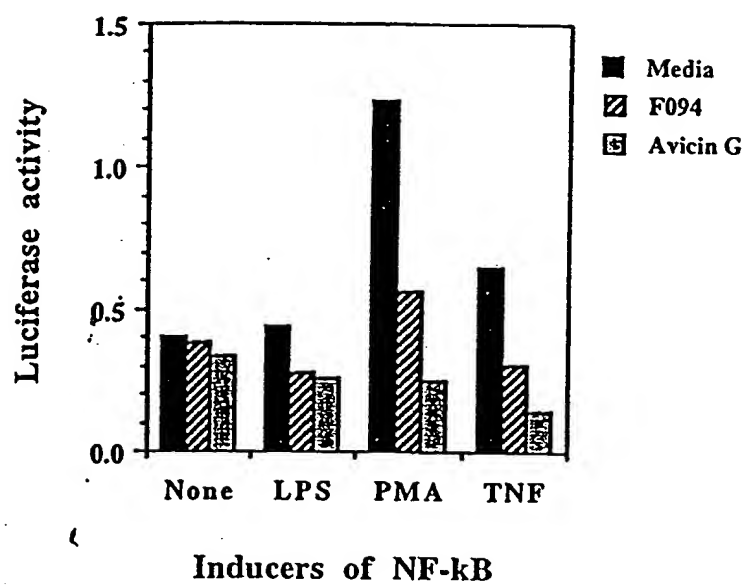


FIG. 54 A, B, C

A



B

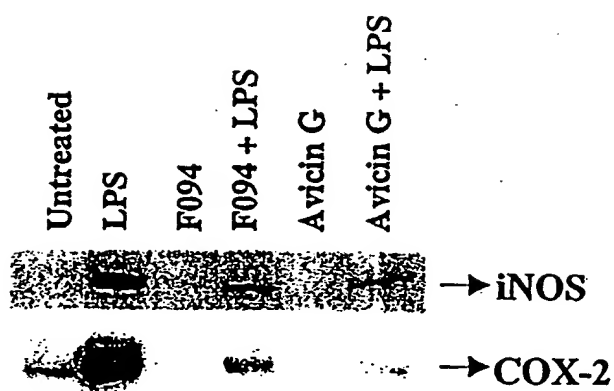
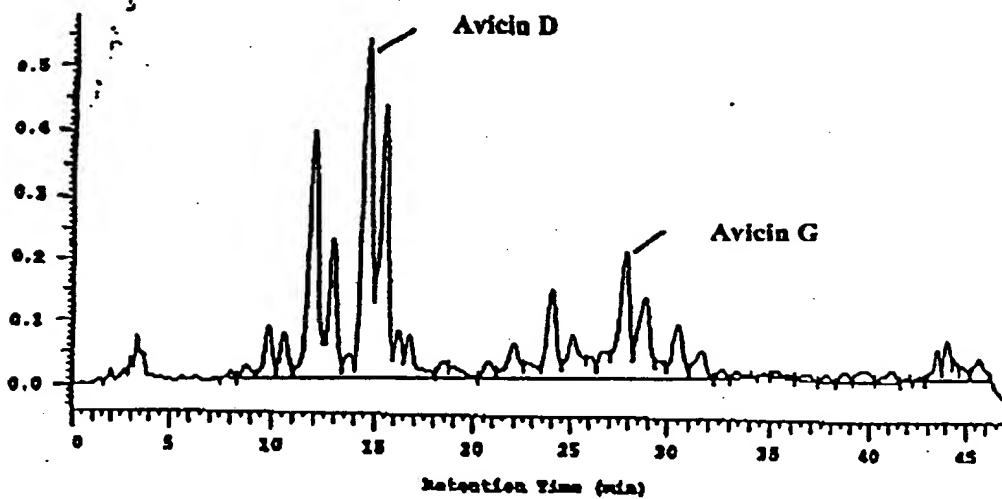


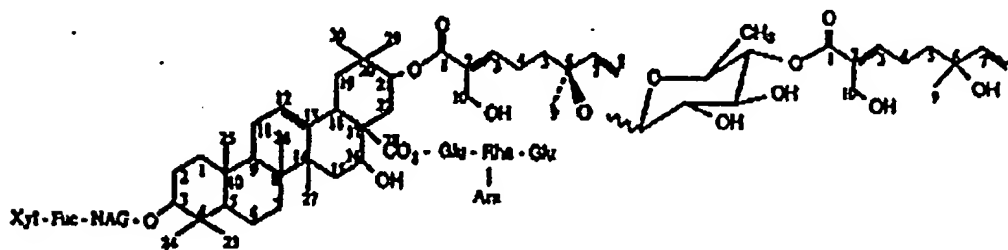
FIG. 55 A, B



IC₅₀ Values

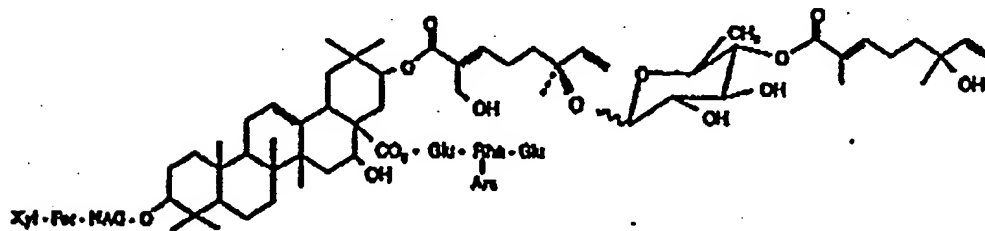
HPLC Separation of the Avicins in F094

0.331-0.407 $\mu\text{g/ml}$



Avicin D

0.320-0.326 $\mu\text{g/ml}$

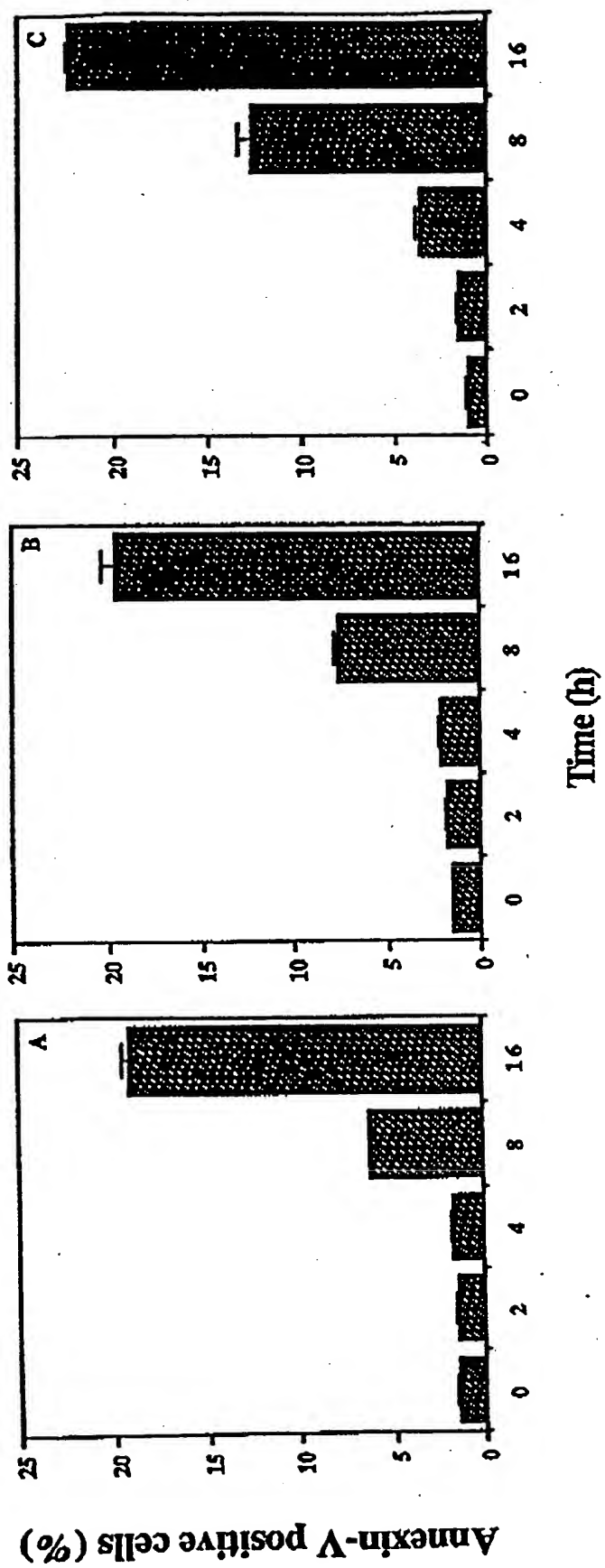


Avicin G

0.160-0.181 $\mu\text{g/ml}$

FIG. 56

FIG. 57

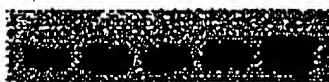


Time (h)	0	0.5	1	2	4
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Mixture

Fold increase **1.0** **0.8** **0.8** **1.3** **1.5**



Avicin D

Fold Increase **1.0 1.5 1.7 1.9 3.5**




Avicin G

Fold increase **1.0 3.5 4.7 6.3 8.4**

FIG. 58

Time (min) 0 1 2 5 10 20

 → **Cyt-c**

B

Avidin G ($\mu\text{g/ml}$) 0 0.03 0.12 0.5 2 5

→ **Cyt-c**

C

Untreated
DEVD
zVAD-fmk
Avicin G
DEVD+Avicin G
zVAD-fmk+Avicin G

→ Cyt-c

FIG. 59

FIG. 60

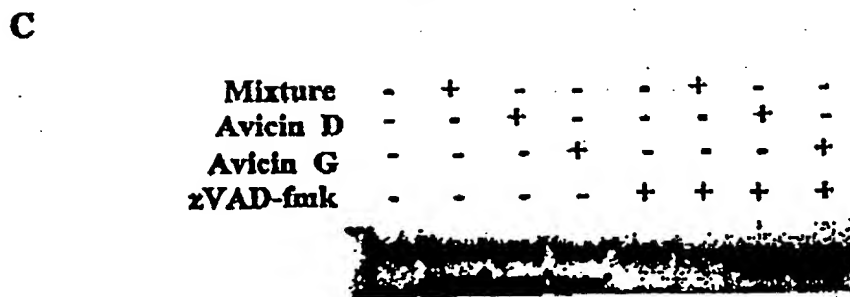
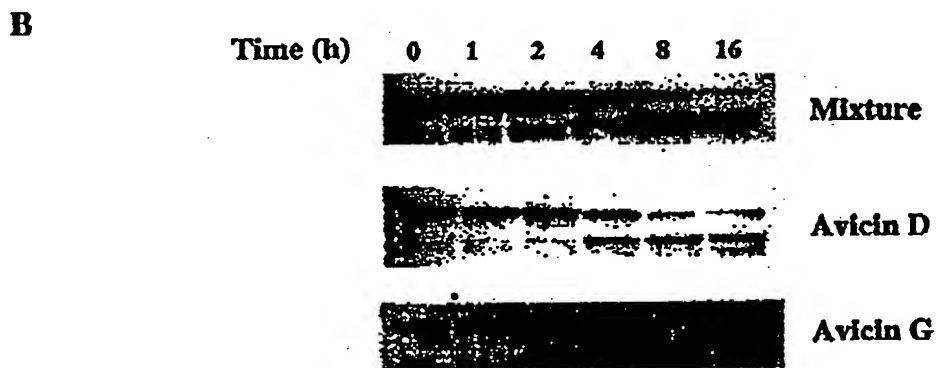
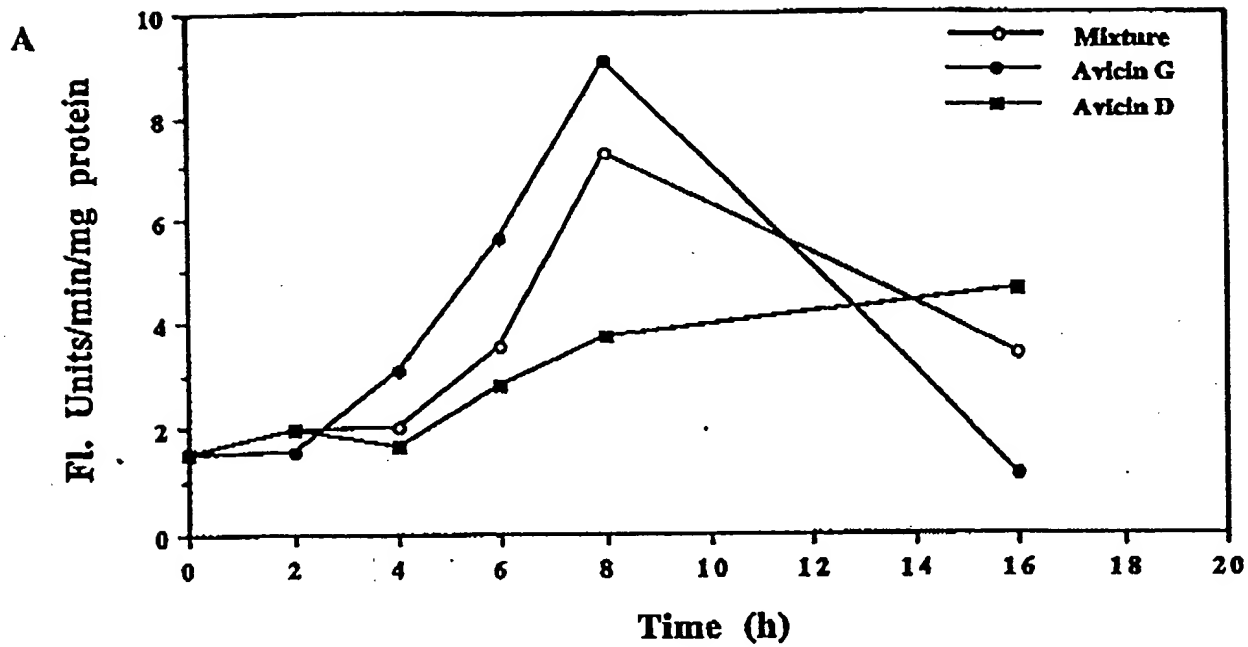


FIG. 60

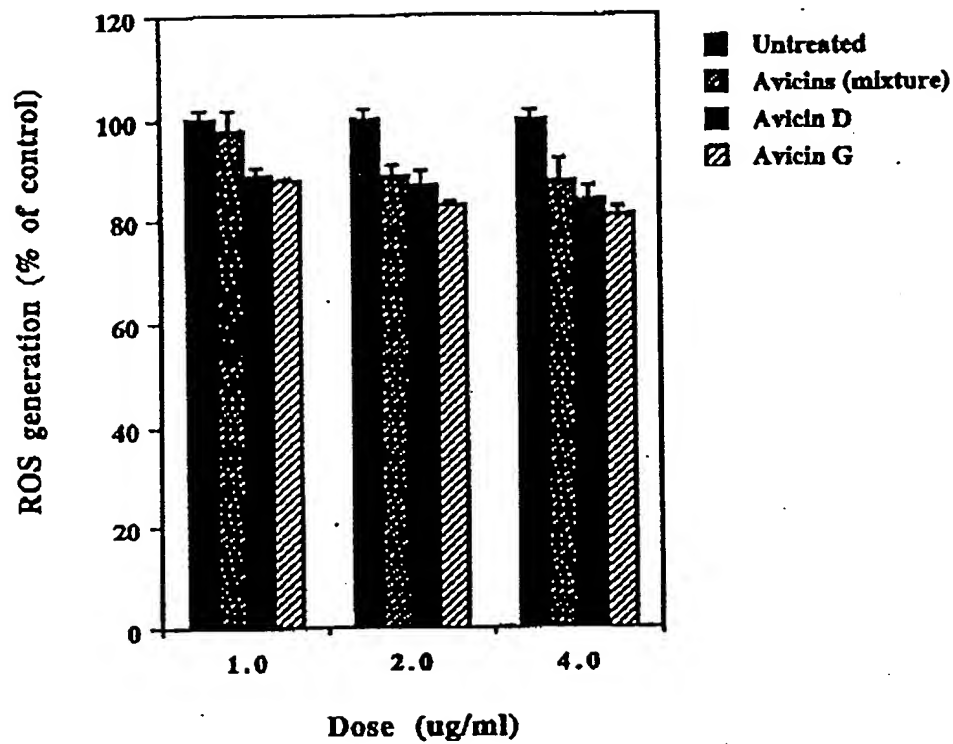


FIG. 62

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